AUGUST 24, 1957 PAGES 349 TO 394

THE LANCET

Dec. 8
6 SEP 1957
Copy

Offices: 7, ADAM STREET, ADELPHI, W.C.2
Telegrams: LANCET, RAND, LONDON Telephone: TEMPLE BAR 7228 and 7229

No. VIII OF VOL. II 1957 LONDON, SATURDAY, AUGUST 24, 1957 Pp. 96—Price 1s. 6d.
No. 6991 VOL. CCLXXIII Founded 1823 PUBLISHED WEEKLY Registered as a Newspaper Annual Subscription: £3 3s.

"SOROSIL"

DERMAL OINTMENT

for the amelioration of itching in Pruritus, Prurigo, and other inflammatory skin conditions

H. R. NAPP LIMITED

3 & 4, CLEMENTS INN LONDON, W.C.2

Second Revised Edition

THE DISEASES OF OCCUPATIONS

By DONALD HUNTER, C.B.E., M.D., F.R.C.P.
Physician, The London Hospital, Director of Department for Research in Industrial Medicine (Medical Research Council).

"A Volume which far outshines in knowledge and in experience anything that has been produced before in this enormous field. It will become the standard work on the subject for a long time to come."—*The British Medical Journal.*

1080 pages £5 5s. net, plus 2s. postage

The English Universities Press Ltd., 102, Newgate-street, London, E.C.1

MANAGEMENT OF BURNS

Six articles prepared by a subcommittee of the BRITISH ASSOCIATION OF PLASTIC SURGEONS
Reprinted from THE LANCET *with an appendix*

These articles record the practice of surgeons who are treating burns every day and who see the good results of treatment that is carefully planned from the start. Here is their plan, fully but briefly set out.

48 pages Price 2s. 6d. (postage 4d.)

The Lancet Limited, 7, Adam-street, Adelphi, London, W.C.2

CAREERS IN MEDICINE

Edited by P. O. WILLIAMS, M.A. (Cantab.), M.B., B.Chir., M.R.C.P.

With contributions from 49 eminent medical authorities

Cr. 8vo 292 pages Price 15s. net, plus 1s. 4d. postage

This book outlines the particular qualities of mind, the type and amount of specialised training, required in each branch of the Medical Profession.

"... it should be in the hands of everyone who has to advise medical students, and certainly should be consulted by every newly-qualified doctor."—*The Practitioner.*

Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

Third Edition

ABDOMINAL OPERATIONS

By RODNEY MAINGOT, F.R.C.S.
Surgeon, Royal Free Hospital

Completely revised. 74 Chapters (11 new). 1594 Illustrations. 11 Colour Plates. 1568 Pages. Price £8 10s. net.

H. K. Lewis & Co. Ltd., 136, Gower-street, W.C.1

TECHNIQUES IN PHYSIOTHERAPY

Edited by
F. L. GREENHILL, S.R.N., M.C.S.P., T.H.T.
late Sister-in-Charge, Medical Rehabilitation Unit, Royal Free Hospital; late Sister-in-Charge, Rehabilitation Unit, Hill End E.M.S. Hospital (St. Bartholomew's); Former Member Council of Chartered Society of Physiotherapy.

Assisted by
C. B. HEALD, C.B.E., M.D., F.R.C.P., in Rheumatism and Arthritis.
J. N. BARRON, F.R.C.S., in Burns and Injuries of the Hand.
Mr. J. COLSON, M.C.S.P., M.A.O.T., Occupational Therapy in Medicine and Surgery.

Demy 8vo Pages 222 + x 8 plates 34 figures
12s. 6d. net, plus 1s. 2d. postage.

Hodder & Stoughton Ltd., 20, Warwick-square, London, E.C.4

Sixth Edition *Now available*

PRINCIPLES OF MEDICAL STATISTICS

By A. BRADFORD HILL, C.B.E., D.Sc., Ph.D., F.R.S.

Demy 8vo 314 + x 10s. 6d. net, plus 10d. postage

Revised and enlarged (containing a new chapter on Clinical Trials and 16 pages of random sampling numbers).

The Lancet Limited, 7, Adam-street, Adelphi, London, W.C.2.

UNITED STATES OF AMERICA AND CANADIAN SELLING RIGHTS HELD BY OXFORD UNIVERSITY PRESS, INC.
114, Fifth Avenue, New York, 11, N.Y., U.S.A.

NEW AUGUST PUBLICATIONS

STUDIES ON FERTILITY—VIII (1956)
Edited by R. G. HARRISON.
160 pages, 34 illustrations. 25s.

OCCIPITO POSTERIOR POSITIONS
By E. L. KING. 128 pages, 84 illustrations. 27s. 6d.

THE HUMAN BRAIN: From Primitive to Modern
By A. M. LASSEK. 232 pages. 36s.

INHALATION ANALGESIA IN CHILDBIRTH
By E. H. SEWARD and R. BRYCE-SMITH.
64 pages, 10 illustrations. 7s. 6d.

SEX PERVERSIONS AND SEX CRIMES
By J. M. REINHARDT. 288 pages. 43s.

PNEUMOENCEPHALOGRAPHY
By E. GRAEME ROBERTSON.
502 pages, 596 illustrations. £5 10s.

BLACKWELL SCIENTIFIC PUBLICATIONS · OXFORD

Analgesics

The introduction of Proponesin following development of the active substance—tolpronine hydrochloride—in the B.D.H. research laboratories has widened the effective range of B.D.H. analgesics.

A logical addition to the B.D.H. range

'PROPONESIN'
TRADE MARK

TABLETS OF TOLPRONINE HYDROCHLORIDE

Provide quick-acting, short term effects against the pain of herpes zoster, dysmenorrhoea, toothache, headache, sinusitis and backache.

Each tablet contains 100 mg. of active substance.
Basic N.H.S. prices: Bottle of 10 at 1/8;
50 at 5/-; 250 at 17/6, purchase tax extra.

'TERCIN' TABLETS
TRADE MARK

Remain the preparation of choice in treatment of the joint pains of influenza and arthritic conditions generally.

Each tablet contains: Aspirin 5 gr. Phenacetin 3 gr. and butobarbitone ½ gr.
Basic N.H.S. prices: Bottle of 200 at 4/10 and 1,000 at 24/-.

Literature and specimen packings will gladly be sent, on request

Medical Department
THE BRITISH DRUG HOUSES LIMITED · LONDON N.1

AUGUST 24, 1957 PAGES 349 TO 394

THE LANCET

A JOURNAL OF BRITISH AND FOREIGN MEDICINE, SURGERY, OBSTETRICS, PHYSIOLOGY, PATHOLOGY, PHARMACOLOGY, PUBLIC HEALTH, AND NEWS

No. 6991 LONDON: SATURDAY, AUGUST 24, 1957 CCLXXIII

CONTENTS

THE WHOLE OF THE LITERARY MATTER IN THE LANCET IS COPYRIGHT

ORIGINAL ARTICLES

Involvement of the Nervous System in Behçet's Syndrome — A. D. EVANS, M.B., C. A. PALLIS, M.R.C.P., J. D. SPILLANE, F.R.C.P. 349

Encephalomyelopathy in Behçet's Disease — W. H. MCMENEMEY, F.R.C.P., BERYL J. LAWRENCE, M.B. 353

Cellulitis and Thrombophlebitis in Behçet's Syndrome — G. R. CARR, F.R.C.S. 358

The Toxicity and Fate of Injected Animal Antihæmophilic Globulin — A. A. SHARP, M.B., E. BIDWELL, PH.D. 359

Dental Extraction in Hæmophilia — C. WISHART, F.D.S.R.C.S., C. ANNAND SMITH, L.D.S.R.C.S.E., G. E. HONEY, M.R.C.P., K. B. TAYLOR, M.R.C.P. 363

Lipæmia, Heparin, and Blood Viscosity — WILLIAM C. WATSON, M.R.C.P. 366

Use of Glucose Oxidase, Peroxidase, and O-Dianisidine in Determination of Blood and Urinary Glucose — Prof. A. ST. G. HUGGETT, M.B., D. A. NIXON, M.SC. 368

New Method of Studying the Bacterial Flora of Infected Open Wounds and Burns — R. H. GORRILL, M.D., E. J. K. PENIKETT, M.B. 370

NEW INVENTIONS

Tracheostomy Tube and Connections for Patients Having Intermittent Positive-pressure Respiration — JOHN BULLOUGH, F.F.A.R.C.S. 372

Apparatus for Resuscitation and Suction — HENNING RUBEN, CAND. MED., ARNE RUBEN, MED. LIC. 373

IN ENGLAND NOW

A Running Commentary by Peripatetic Correspondents 382

LEADING ARTICLES

PREVENTION OF MATERNAL DEATHS 375

CONTROL OF HÆMOPHILIC BLEEDING 376

MENTAL DEFECT, TETRAPLEGIA, AND ICHTHYOSIS 377

ANNOTATIONS

Polluted Coasts 378

B.C.G. Vaccine 378

An Oral Diuretic 379

Necrosing Polyarteritis in Rheumatoid Arthritis 379

Bronchial Adenoma 380

PUBLIC HEALTH

Tuberculosis Case-finding in the Aged — O. D. BERESFORD, M.R.C.P. 381

Poliomyelitis 381

Influenza 381

PERSONAL PAPERS

Matriarchy 392

LETTERS TO THE EDITOR

The Teaching Hospitals (Mr. B. Lees Read, A.C.A.) 383

Treatment of Hirschsprung's Disease (Mr. G. G. Wyllie, F.R.C.S.) 383

Eclampsia (Dr. K. D. Salzmann) 383

Painful Experiments on Animals (Mr. W. Risdon) 384

Diet and Coronary Thrombosis (Mr. R. Cobb, B.SC.) 384

Blood-counting Machine (Dr. G. A. C. Summers) 384

Cardiac Arrest During Halothane Anæsthesia (Dr. Harold T. Kay) 385

Transfusion Not to Blame (Dr. R. Aidin) 385

Hexylresorcinol in the Treatment of Arthritis (Dr. E. Alfred Lipkin) 385

A New Disease? (Dr. A. F. Roberts; Dr. C. G. A. Thomas) 386

Mortality of Fractures of the Neck of the Femur (Mr. I. M. Stewart, F.R.C.S.E.) 386

Inductotherm in Anuria (Mr. W. W. Woodward, F.R.C.S.) 386

Unnecessary Irradiation in Chest Radiography (Dr. James F. Brailsford) 386

Consultant and Specialist 387

Women in Prison on "Attempted Suicide" Charges (Dr. M. M. Glatt) 387

A Clinic for Homosexuals (Dr. R. H. N. Long) 388

Dihydrocodeine (Dr. Jack Levin) 388

Effect of Certain Protein Foods on Blood-sugar Levels and Glucose Tolerance (Dr. Franklin Bicknell) 388

The State of Development of Newborn African Children (Dr. Frank Falkner) 389

Ileostomy Chemistry (Mr. N. Crawford, F.I.M.L.T., Mr. B. N. Brooke, F.R.C.S.) 389

Radiation and Leukæmia (Dr. W. M. Court Brown, Dr. Richard Doll) 389

The Newborn Infant's Oxygen-supply (Dr. William A. Silverman, Dr. Masako Nishihara) .. 390

Penicillin Treatment of Leptospirosis (Dr. Lewis Cloin) 390

High-pressure Oxygen and Radiotherapy (Dr. Cyril Sanger) 390

Reflections on Medical Travel (Dr. Ali Muhammad) 391

Vitamin Supplementation (Dr. R. M. Dykes) 391

Generation Death-rates and Tuberculosis (Dr. H. O. Lancaster) 391

p-Aminosalicylic Acid in the Treatment of Thrombophlebitis (Dr. J. C. Annand) 392

A Case of Mistaken Identity (Dr. Geoffrey Bourne) 392

REVIEWS

Notices of Books 374

OBITUARY

Arthur John Jex-Blake 393

Eric Arnold Scott 393

NOTES AND NEWS

Charing Cross Hospital 394

A Danish Centenary 394

Surgeons' Battle 394

'ANCOLAN'

TRADE MARK

Tablets containing 25 mg. meclozine dihydrochloride

THE B.D.H. ANTIHISTAMINIC

IN HAY FEVER *and other allergic conditions and* **MOTION SICKNESS**

ADVANTAGES long duration of action exceptionally well tolerated

Basic N.H.S. prices: Plastic container of 10 tablets 1/8
Bottles of 25 tablets 3/8
" " 250 " 32/6

Literature and samples will be sent on request

THE BRITISH DRUG HOUSES LTD. (Medical Dept.) LONDON N.1

Alpha tocopherol (Vitamin E) for CARDIOVASCULAR-RENAL DISEASES

The natural vitamin E available only since 1948 must not be confused with the wheat germ oil in use before that date with its limitations as to potency and stability.

The natural vitamin E of today comprises a concentrate distilled from the oils of cottonseed, palm, soya bean, etc.

The standard laid down by the League of Nations is that 1 international unit = 1 mgm. of d.l. *alpha* tocopheryl acetate.

The VITA-E Gelucap (75 i.u.) heads the list of brands approved by the Vitamin E Society and is that recommended by the Shute Foundation for Medical Research and used with such conspicuous success at the Shute Institute.

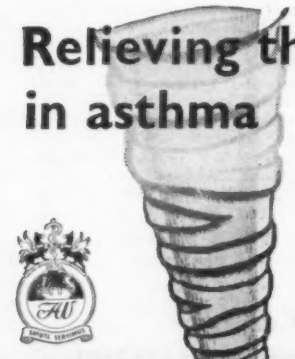
LITERATURE ON REQUEST

Sole Manufacturers:

THE BIOGLAN LABORATORIES LTD.
HERTFORD, HERTS, ENGLAND.

Specialists in Hormones and Vitamins

Relieving the bronchial tree in asthma



'ASMAC' TABLETS are formularized to provide symptomatic relief of the bronchial tree both during actual dyspnoeic attacks of bronchial asthma, and during remissions.

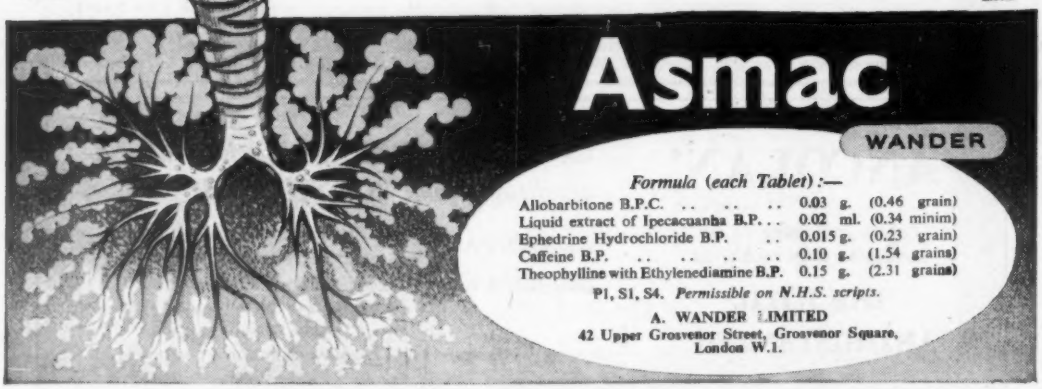
'Asmac' Tablets combine in a single prescription 'official' drugs recognized for their reliability to effect mental sedation, decongestion, expectoration and bronchodilatation.

Packs and Cost to Pharmacists:

Standard Tube of 20, 3/-

Dispensing Bottles:
100, 12/-; 500, 52/6; 1000, 102/6

M372.



Asmac

WANDER

Formula (each Tablet):—

Allobarbitone B.P.C.	0.03 g.	(0.46 grain)
Liquid extract of Ipecacuanha B.P.	0.02 ml.	(0.34 minim)
Ephedrine Hydrochloride B.P.	0.015 g.	(0.23 grain)
Caffeine B.P.	0.10 g.	(1.54 grains)
Theophylline with Ethylenediamine B.P.	0.15 g.	(2.31 grains)

P1, S1, S4. *Permissible on N.H.S. scripts.*

A. WANDER LIMITED
42 Upper Grosvenor Street, Grosvenor Square, London W.1.

*Xylocaine**

BRAND OF
LIGNOCAINE HCl
B.P. AND LIGNOCAINE BASE

duncan

for local anaesthesia...

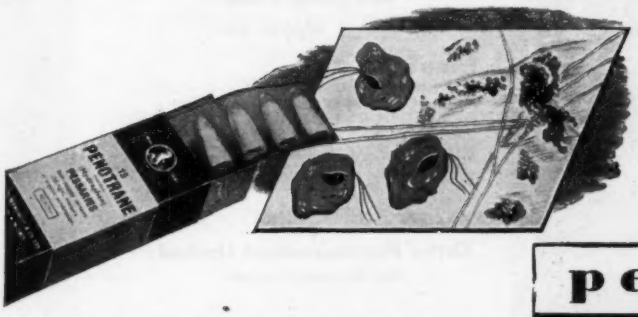
. . . considerable experience has shown this to be the first compound to give clearly better results than procaine in the long search for an improved local anæsthetic. Xylocaine is available as solutions with and without adrenaline in ampoules, cartridges and multidose containers. It is also presented in ointments, lozenges, and a viscous liquid. Crystals of the hydrochloride are available (to hospitals only). It is fully effective for infiltrations and blocks, and on the surface of mucous membranes. Literature about its many uses will be sent on request.

TIME TESTED . . . . STABLE . . . . SAFE

DUNCAN FLOCKHART of Edinburgh

The Doctors' House

**Manufactured in Scotland under licence from A. B. Astra, Sodertalje, Sweden.*



Effective
against both Trichomonas
and Monilia

penotrane

PHENYLMERCURIC DINAPHTHYLMETHANE DISULPHONATE

in vaginal therapy

The powerful trichomonacidal and fungicidal properties of PENOTRANE present the greatest advantage in the treatment of vaginal discharge, particularly trichomonal vaginitis and moniliasis. PENOTRANE is also strongly bactericidal and it deeply penetrates the vaginal mucosa. Both the Pessaries and Vaginal Cream are buffered to approximate the normal vaginal acidity.

INDICATIONS: ★ Vaginal Discharge due to trichomonal, monilial and coccal infections. ★ Pruritus Vulvae. ★ Obstetrical Lubrication. ★ Pre-operative Skin Disinfection.

Literature and professional samples on request.

AVAILABILITY:

PENOTRANE	Applicator Sets—containing Penotrane Vaginal Cream & disposable applicators.
PENOTRANE	Aqueous Solution—Bottles of 100, 500 and 2,000 c.c.
PENOTRANE	Jelly—Tubes of 1 oz.
PENOTRANE	Pessaries—Cartons of 15 and 100.
PENOTRANE	Powder — Polythene Insufflating Containers.
PENOTRANE	Tincture—Bottles of 15, 100, 500 and 2,000 c.c.

WARD, BLENKINSOP & COMPANY, LIMITED

YORK HOUSE, 37, QUEEN SQUARE, LONDON, W.C.1.

Telephone: HOLborn 5992/6 (5 lines.) Telegrams: Duochem, Westcent, London.

A birthright safeguarded . . .
Massé
TRADE MARK
CREAM
in antepartum
nipple conditioning
and postpartum
nipple care
Massé cream contains:
9-amino acridine and allantoin in a
non-greasy, odourless and stainless cream base
Ortho
Ortho Pharmaceutical Limited
High Wycombe • England

Elastoplast

Trade Mark

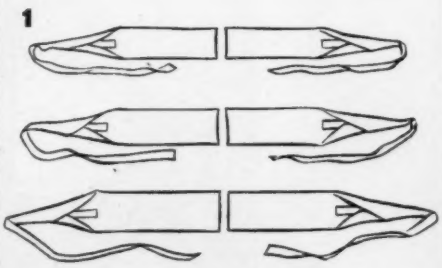
as an alternative to the conventional many-tailed bandage

When frequent dressings are necessary, the following method of applying Elastoplast may be used as a substitute for an abdominal many-tailed bandage.

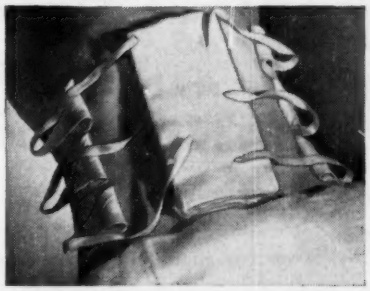
Six pieces, each about 12 inches in length, are prepared from a 3-inch wide Elastoplast bandage. Tapes are attached as illustrated (Fig. 1), and the completed pieces applied to the body from each side (Fig. 2). The tapes are tied over the dressing covering the wound (Fig. 3). The bandage may be applied by one person without disturbing the patient. It is easily made, provides adequate support and will remain firmly in position.

The above method is comfortable in use as the patient does not have to wear perineal stirrups to keep the bandage in place, or to lie on a bandage which may become "rucked-up" — disadvantages associated with the flannelette type of many-tailed bandage.

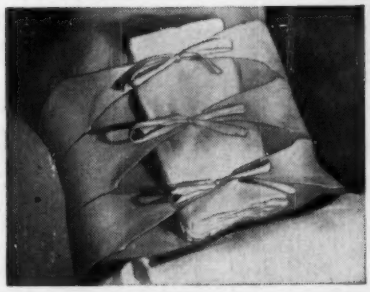
1



2



3



ELASTOPLAST

Elastic adhesive bandages (Porous) B.P.C.

Available in 2″, 2½″, 3″ and 4″ widths by 3 yards (unstretched). Prescribable on form E.C.10.

Elastoplast

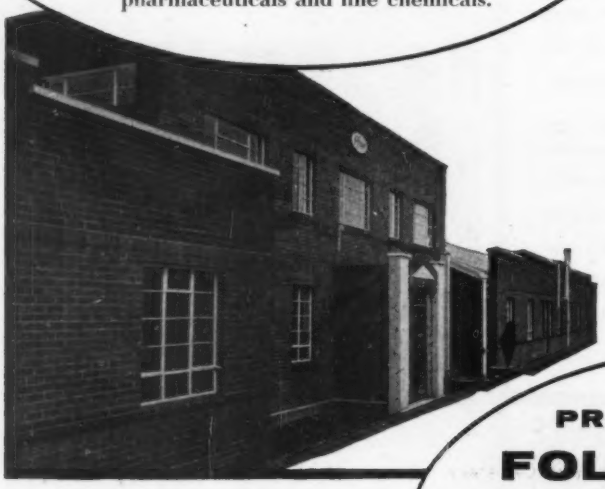
an S&N product

SMITH & NEPHEW LTD · WELWYN GARDEN CITY · HERTS

5

MADE IN SANDWICH

In one of the largest and most modern plants of its kind in Europe, we manufacture both pharmaceuticals and fine chemicals.

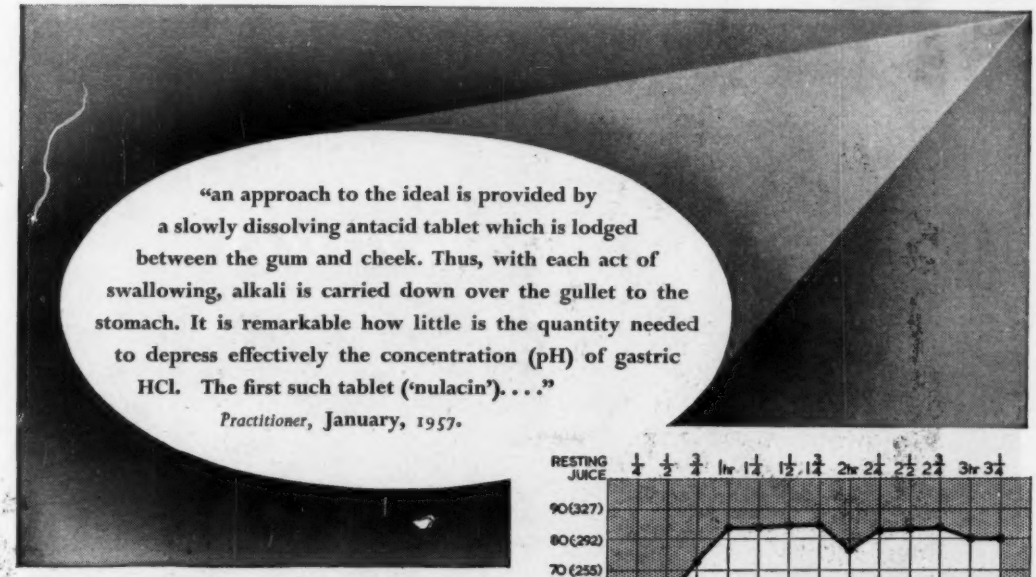


PROCESSED IN FOLKESTONE

In Folkestone we prepare and pack the finished products — tablets, capsules, ointments, injections and other convenient dosage forms.

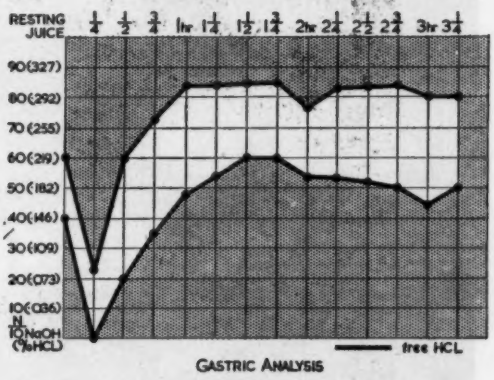
PFIZER PHARMACEUTICALS Pfizer

PFIZER LTD · FOLKESTONE · KENT


"an approach to the ideal is provided by a slowly dissolving antacid tablet which is lodged between the gum and cheek. Thus, with each act of swallowing, alkali is carried down over the gullet to the stomach. It is remarkable how little is the quantity needed to depress effectively the concentration (pH) of gastric HCl. The first such tablet ('nulacin'). . . ."
Practitioner, January, 1957.

NULACIN THERAPY

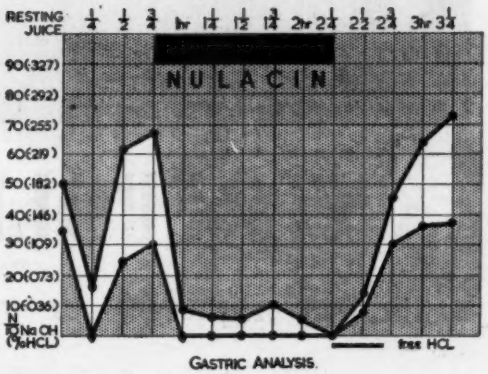
—Simple, safe, effective



GASTRIC ANALYSIS

A Nulacin tablet effectively depresses the concentration of gastric HCl in peptic ulcer and other conditions of hyperacidity. It also provides protection against gastric HCl to the otherwise unprotected oesophageal wall and in such conditions as oesophagitis and hiatus hernia.

SUPPLY. Nulacin tablets may be prescribed on E.C.10. The dispensing pack of 25 tablets is free of Purchase Tax. (Basic price to N.H.S.: 2/-). Also available in tubes of 12.



GASTRIC ANALYSIS

HORLICKS LIMITED *Pharmaceutical Division, Slough, Bucks., England*

BIBLIOGRAPHY

Antacids, *The Practitioner*, January, 1957, **178**: 43

Antacids in Peptic Ulcer, *The Practitioner*, January, 1956, **176**: 103

Recent Advances in the Ulcerative Diseases of the Gastro-intestinal Tract. *Amer. J. Gastro.*, December, 1956, **26**: 665

Ambulatory Continuous Drip Method in the Treatment of Peptic Ulcer, *Amer. J. Dig. Dis.*, March, 1955, **22**: 67-71

Management of Peptic Ulceration in General Practice, *Med. World*, December, 1954, **81**: 591-601

Clinical Investigation into the Action of Antacids, *The Practitioner*, July, 1954, **173**: 46

Further Studies on the Reduction of Gastric Acidity, *Brit. Med. J.*, 23rd January, 1954, **1**: 183-184

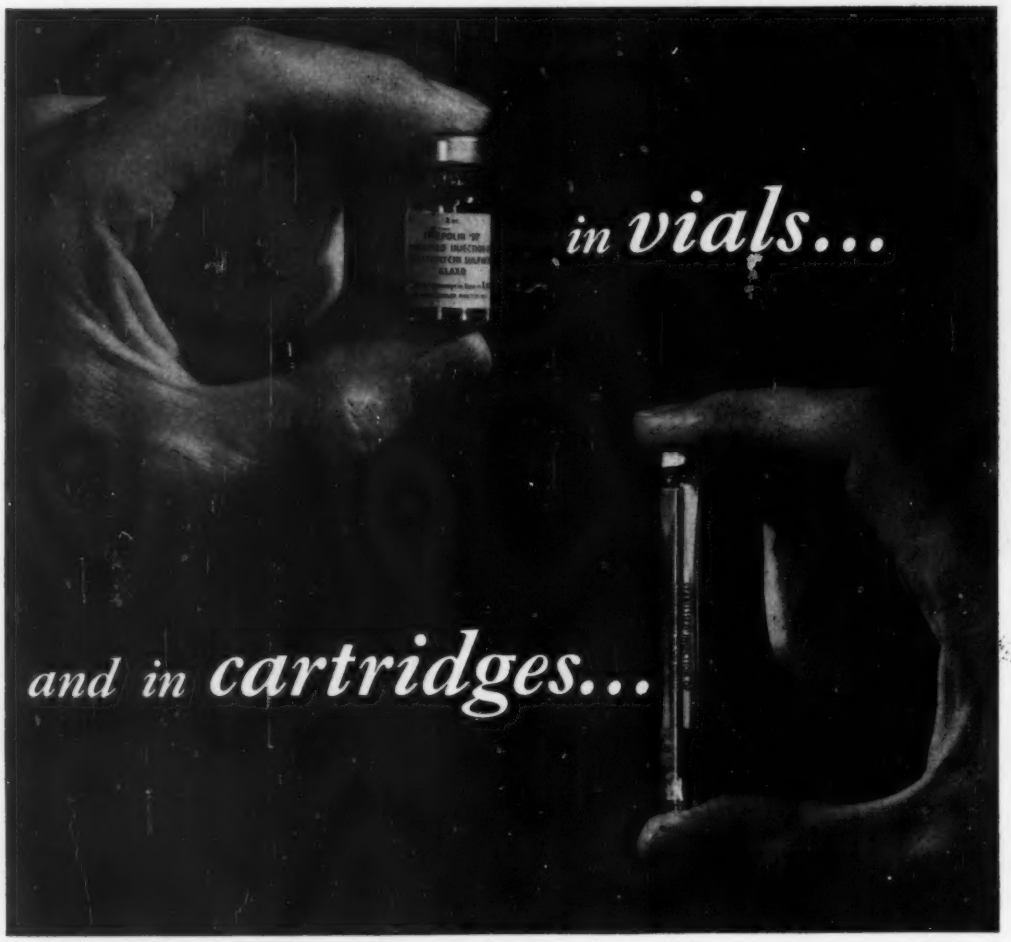
Control of Gastric Acidity by a New Way of Antacid Administration, *J. Lab. Clin. Med.*, 1953, **42**: 955

The Effect on Gastric Acidity of "Nulacin" Tablets, *Med. J. Aust.*, 28th November, 1953, **2**: 823-824

Discussion on Peptic Ulceration, *Proc. Roy. Soc. Med.*, May, 1953, **46**: 354

Medical Treatment of Peptic Ulcer, *Med. Press*, 27th February, 1952, **227**: 195-199

The Control of Gastric Acidity, *Brit. Med. J.*, 26th July, 1952, **2**: 180-182



STREPOLIN 50% (1 gram in 2cc.)

TRADE MARK

STABILISED INJECTION OF STREPTOMYCIN SULPHATE GLAXO

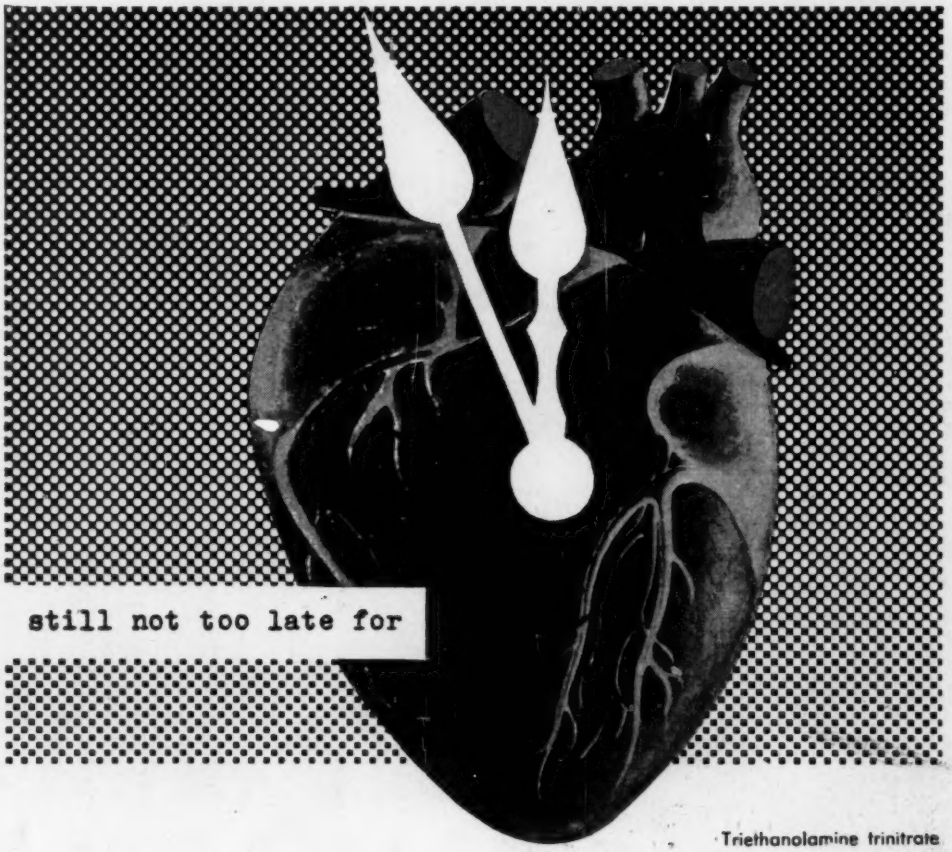
- ★ ready for immediate use
- ★ in 1 gm. and 5 gm. vials, 1 gm. cartridges
- ★ Strepolin '50' cartridges can be used in any commercially available disposable cartridge syringe. The cartridges may be aspirated.

Also available, in vials only: 25% (1 gram in 4cc.) and 33% (1 gram in 3cc.).

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX BYRon 3434

Subsidiary Companies or Agents in most countries.

Angina pectoris



Triethanolamine trinitrate

PRAENITRONA

Prevents attacks of angina pectoris or at least reduces the severity and frequency of attacks

For maintenance treatment, 1 – 2 tablets 3 or 4 times a day
Packings: 50 · 500 · 1000 tablets, each of 1 mg.

Praenitrona is prescribable on N. H. S. Form E. C. 10

SCHERING A. G. BERLIN / GERMANY

Samples and literature are available upon request from the sole distributors for the U.K.:
Pharmethicals (London) Ltd., 20, Gerrard Street, London, W. 1

Get two on the job—that's better!

THE TWO active ingredients in 'Sulmezil' V work better together than either used alone.

One ingredient is penicillin V, the acid stable form of penicillin which is rapidly and efficiently absorbed and gives consistent and reliable blood levels. This form of penicillin has proved to be markedly superior in these respects to other oral penicillin preparations.

Combined with penicillin V is 'Sulphamezathine', which has been widely accepted for many years on account of its high potency coupled with low toxicity. It is undoubtedly the best sulphonamide for routine use.

'Sulmezil' V tablets present these two drugs in a single easily-administered form. Each tablet contains 60 mg. of penicillin V (Calcium Salt) and 0.5 g. of 'Sulphamezathine'. In packs of 25, 100 and 500.

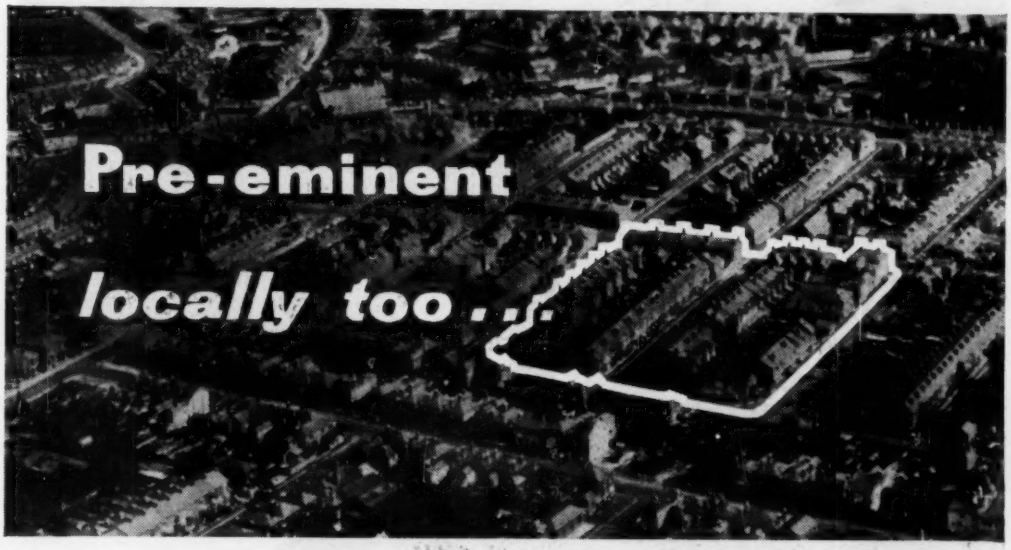
'Sulmezil' V tablets

IMPERIAL CHEMICAL INDUSTRIES LIMITED Pharmaceuticals Division Wilmslow Cheshire

ICI

Ph.746

10



ACHROMYCIN tetracycline is unsurpassed among broad-spectrum antibiotics. Not only is this true in severe generalized infections but in the strictly localized conditions too, where topical application of the drug can be relied upon to exert intensive antibacterial action – right at the site of infection – with gratifying certainty and with the minimum of side reactions. This valuable property of ACHROMYCIN has led to the formulation of a comprehensive range of topical presentations – each with a well defined place and purpose in general and hospital practice.

ACHROMYCIN*

*REGD. TRADE MARK

TETRACYCLINE

CYANAMID 1907 50 1957

SKIN INFECTIONS - ACHROMYCIN Ointment 3%
EYE INFECTIONS - ACHROMYCIN Ophthalmic Ointment 1%
ACHROMYCIN Ophthalmic Powder Sterilised
EAR INFECTIONS - ACHROMYCIN for Ear Solution
THROAT INFECTIONS - ACHROMYCIN Troches

LEDERLE LABORATORIES DIVISION
Cyanamid OF GREAT BRITAIN LTD., London, W.C.2

Boots

'Hydrocortistab'

TOPICAL HYDROCORTISONE PREPARATIONS

A comprehensive range to meet every requirement in dermatological and ophthalmological practice

Skin ointment
Eye ointment
Eye drops
Cream
Lotion

'Hydromycin'

HYDROCORTISONE AND NEOMYCIN

Skin ointment
Ear/Eye ointment
Ear/Eye drops

Full details of strengths and sizes gladly sent on request

BOOTS PURE DRUG COMPANY LTD. NOTTINGHAM ENGLAND

8272

Relief of Rheumatic Pain in General Practice

1. *Formulation of succinate overcomes toxicity of massive dosage of aspirin*

Pain caused by all forms of rheumatism can now be relieved promptly by massive aspirin dosage *without fear of toxicity*. The Berex formulation of aspirin (3.7 gr.) and calcium succinate (2.8 gr.) has overcome this old problem so effectively that your patients can safely administer the drug themselves. Repeated visits to the surgery for supervision of administration are unnecessary.

2. *Side-effects fewer and milder*

Even after prolonged dosage, Berex produces no toxic effects. The prothrombin level is maintained and there is no hæmorrhagic tendency.* Prolonged periods of relief can be enjoyed in safety. The patient is simply instructed to reduce the initial high dosage as soon as the pain diminishes. Side effects, if present at all, are fewer and milder.

3. *Encourages tissue respiration*

Experimentally, by Warburg test, it has been shown that the inhibitory action of salicylate on tissue respiration is completely offset when it is combined with succinate. Succinate encourages cellular respiration and stimulates the respiratory enzyme systems. It is to this stimulating action that the beneficial effect of succinate is attributed.

* "*No abnormal prolongation of prothrombin time even after 68 days of succinate-salicylate.*" "*The results also show that this succinate-salicylate formulation combines safety and efficacy, permitting wide use both for treatment and maintenance without the excessive supervision required in many other forms of therapy.*"
Delaware State Med. J., 1954, 26, 22.

BEREX Trade Mark

PROMPT RELIEF of all rheumatic pains by massive aspirin dosage is now made safe by the Berex succinate-aspirin formulation. Prolonged dosage does not lower the prothrombin level, and does not therefore produce hæmorrhagic tendency.

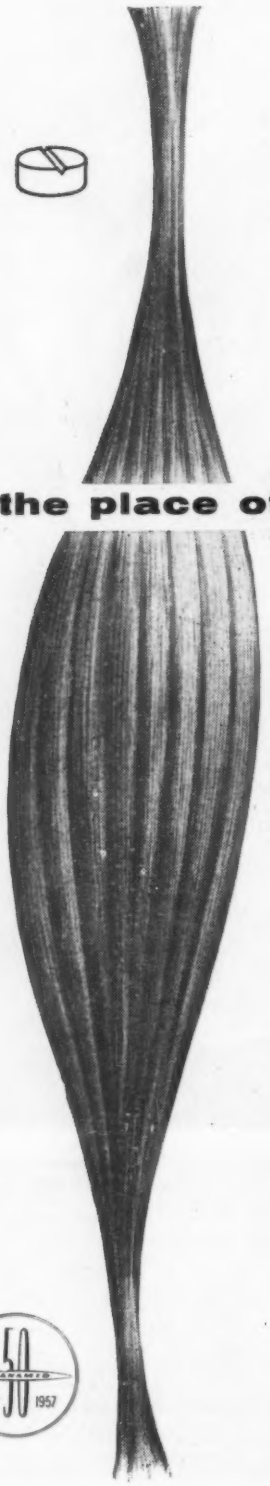
FOR PROMPT RELIEF OF PAIN ASSOCIATED WITH ALL FORMS OF RHEUMATISM

FORMULA:
Calcium succinate 2.8 gr., acetylsalicylic acid 3.7 gr.
IN TABLET FORM:
basic N.H.S. price, 4/8½d.–100 tablets; 24/3d.–600 tablets.

BEREX HAS NEVER BEEN ADVERTISED TO THE PUBLIC

A professional sample will be sent on request to:
MEDICAL DEPARTMENT:
CLINOD PHARMACEUTICALS LTD., BELVUE RD., NORTHOLT, GREENFORD, M UDX.

13



the place of Miltown®

MEPROBAMATE

in rheumatic diseases

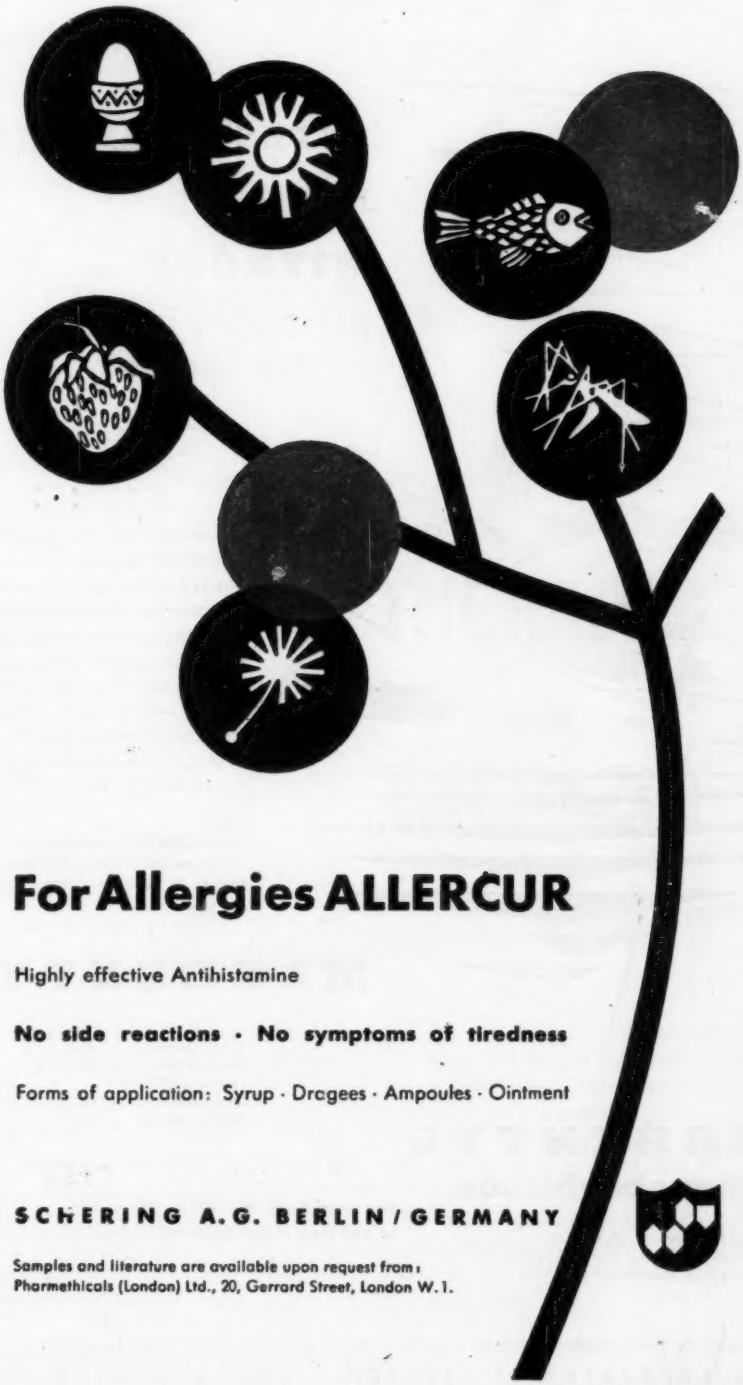
The value of MILTOWN in the relief of common rheumatic diseases is becoming more evident as results of clinical work are published. Satisfactory relief of muscle stiffness and pain has been observed in a high proportion of patients with various rheumatic conditions with a predominance of fibrositic symptoms. Impressive results have also been achieved in rheumatoid spondylitis, cervical root syndrome and mild rheumatoid arthritis. The promptness of relief following MILTOWN in these conditions has been particularly notable. MILTOWN is effective orally—typical dosage in rheumatic conditions being one tablet (400 mg.) three or four times daily.

MILTOWN is presented in tablets of 400 mg. Bottles of 50 and 500

®TRADE MARK OF CARTER PRODUCTS INC.

LEDERLE LABORATORIES DIVISION

Cyanamid OF GREAT BRITAIN LTD., London, W.C.2



For Allergies ALLERCUR

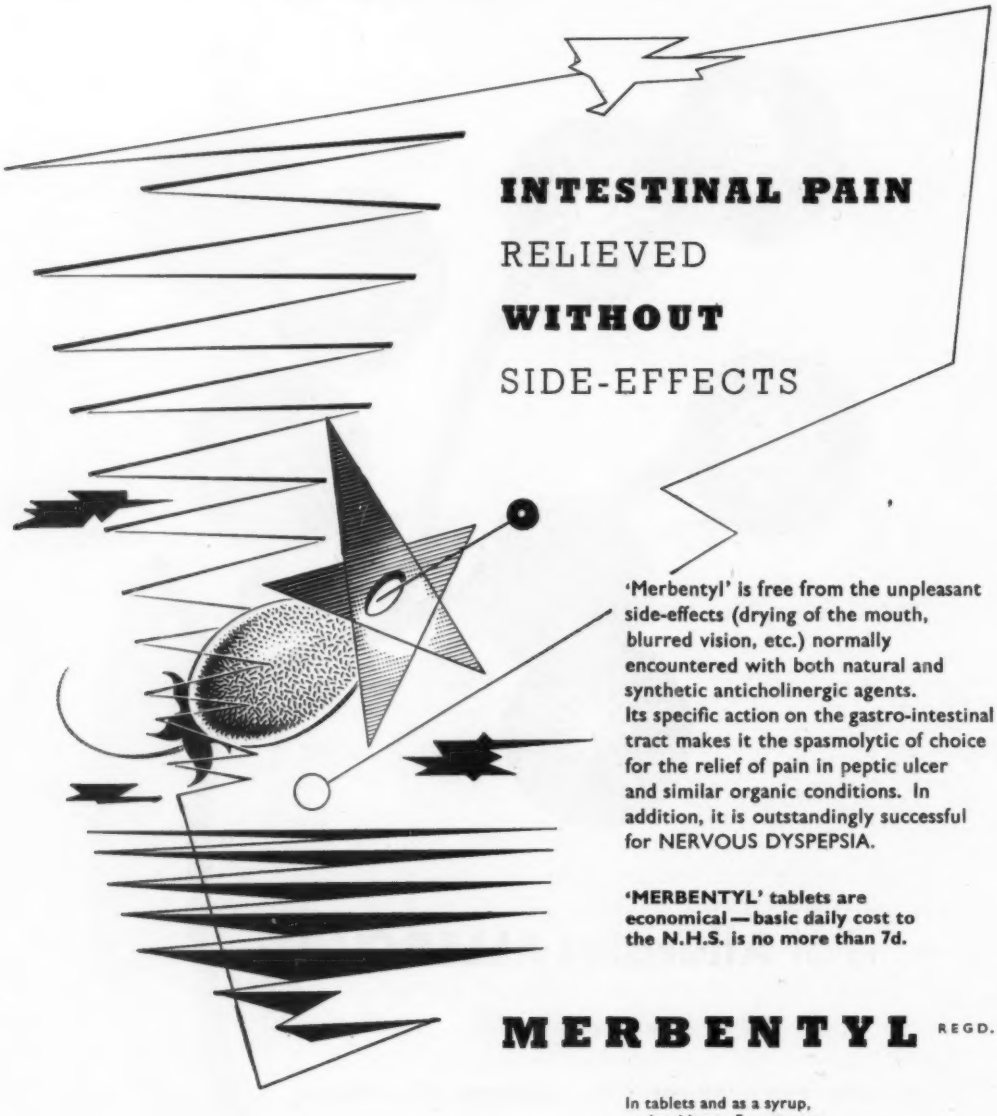
Highly effective Antihistamine

No side reactions · No symptoms of tiredness

Forms of application: Syrup · Dragees · Ampoules · Ointment

SCHERING A.G. BERLIN / GERMANY

Samples and literature are available upon request from:
Pharmethicals (London) Ltd., 20, Gerrard Street, London W.1.



INTESTINAL PAIN
RELIEVED
WITHOUT
SIDE-EFFECTS

'Merbentyl' is free from the unpleasant side-effects (drying of the mouth, blurred vision, etc.) normally encountered with both natural and synthetic anticholinergic agents. Its specific action on the gastro-intestinal tract makes it the spasmolytic of choice for the relief of pain in peptic ulcer and similar organic conditions. In addition, it is outstandingly successful for NERVOUS DYSPEPSIA.

'MERBENTYL' tablets are economical — basic daily cost to the N.H.S. is no more than 7d.

MERBENTYL REGD.

In tablets and as a syrup, each tablet or 5 c.c. syrup containing 10 mg. diethylaminocarbethoxybicyclohexyl hydrochloride.

MERBENTYL
with Phenobarbitone

in tablets and as a syrup, each tablet or 5 c.c. syrup containing 10 mg. 'Merbentyl' and 15 mg. (gr. ¼) phenobarbitone.

For conditions requiring sedation in addition to antispasmodic therapy.

Merrell research

'MERBENTYL' and 'MERBENTYL' WITH PHENOBARBITONE *are distributed in the United Kingdom and Eire by*

RIKER LABORATORIES LIMITED · LOUGHBOROUGH · LEICS.

for the Wm. S. Merrell Company, London

Further refinements in the chemotherapy of tuberculosis

THERAPAS

(Calcium B-P.A.S.)

and

THERAZID

('Therapas' and isoniazid)

If P.A.S. is indicated, THERAPAS may be used as the drug of choice because it has these significant properties.

★ No unpleasant taste
★ Overcomes the problems of nausea and vomiting
★ Minimises gastro-intestinal disturbances
★ Breaks down in the body to yield P.A.S.
★ Yields more prolonged blood levels of P.A.S. than an equivalent dosage of P.A.S.
★ Produces high urinary concentrations of P.A.S. and is the drug of choice in the management of genito-urinary tuberculosis.

THERAZID is a convenient and easy to take combination of 'Therapas' and 'Pycazide' (Smith & Nephew's name for isoniazid B.P.) For *domiciliary treatment* THERAZID is particularly valuable. Patients complaining of gastro-intestinal upset and monotony of dosage of P.A.S. and isoniazid therapy will be happier and more co-operative on THERAZID.

S&N products

Further details will gladly be sent on request

SMITH & NEPHEW PHARMACEUTICALS LTD • WELWYN GARDEN CITY • HERTS

RASTINON

»HOECHST«
TOLBUTAMIDE

An oral treatment for diabetes mellitus

EXTENSIVE CLINICAL TRIALS in many countries have shown that Rastinon »Hoechst« tablets provide effective oral treatment for certain types of diabetes mellitus. The initial selection and stabilization of patients to Rastinon therapy should be carried out under strict medical supervision.

Only certain diabetic patients are suitable for treatment with Rastinon »Hoechst«; Tolbutamide.

Each Rastinon tablet contains 0.5 G. of N-Butyl-N¹-toluene-p-sulphonylurea (Tolbutamide). Rastinon »Hoechst« was originated in the research laboratory of Farbwerke Hoechst AG., of Frankfurt, under the laboratory number D.860.

Rastinon is now available on form E.C.10 for those patients *who have been stabilized under strict medical supervision.*

HOECHST PHARMACEUTICALS LIMITED

SLOUGH

Distributed in the United Kingdom by

HORLICKS LIMITED · SLOUGH · BUCKS

from whom further information may be obtained on request

Serpasil

(the alkaloid reserpine from Rauwolfia)

ANTIHYPERTENSIVE

GRADUAL AND SUSTAINED REDUCTION

OF BLOOD PRESSURE

SYNERGISTIC EFFECT WITH OTHER

ANTIHYPERTENSIVES

MODERATE SLOWING OF HEART-RATE

CALMING EFFECT

Tablets of 0.1 mg. and 0.25 mg. in bottles of 25, 100 and 500. Elixir containing 0.25 mg./5 c.cm. in bottles of 100 c.cm. 1 mg. and 4 mg. tablets, 1 mg. and 2.5 mg. ampoules also available.

C I B A

'Serpasil' is a registered trade mark. Reg. user

CIBA LABORATORIES LIMITED, HORSHAM, SUSSEX

Telephone: Horsham 4321. Telegrams: Cibalabs, Horsham.

8/6

Well in the lead...

This EFFECTIVE oral penicillin, Penicillin-V Lilly, has been proved by extensive clinical use to give results comparable with parenteral penicillin.

Available as
'Pulvules' 125 mg. and 250 mg.
and
Suspension 62.5 mg. per teaspoonful.

Also as TABLETS and SUSPENSION Penicillin-V-Sulpha Lilly.

PENICILLIN-V-LILLY

A *Lilly* DISCOVERY

ELI LILLY AND COMPANY LIMITED, BASINGSTOKE, ENGLAND

'migril' for

3D relief in migraine

Dispels headache

Disperses visual disturbances

Defeats nausea and vomiting

'Migril' provides, for the first time, a successful 3-way attack on migraine.

'Migril' contains ergotamine tartrate (2 mgm.), caffeine (100 mgm.) and cyclizine hydrochloride (50 mgm.) in each tablet. The inclusion of cyclizine hydrochloride not only eliminates the nausea and vomiting often associated with migraine but also **enables larger and more effective doses of ergotamine to be administered.**

'migril' BRAND

Ergotamine Compound *(Compressed)*

PACKS OF 10 AND 100

BURROUGHS WELLCOME & CO. (THE WELLCOME FOUNDATION LTD.) LONDON

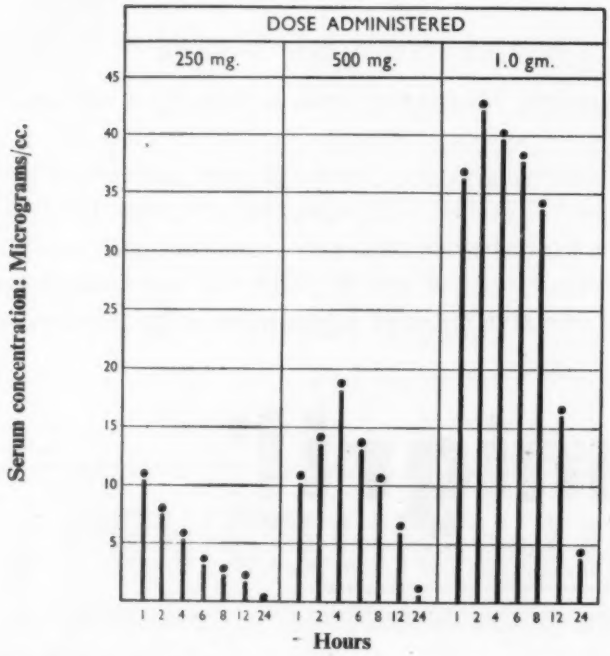
The most powerful challenge yet to resistant staphylococci

BIOTEXIN

Glaxo Novobiocin

- ★ Selective in action
- ★ Extremely well absorbed following oral administration
- ★ Swiftly gives antibacterial concentrations in the blood far exceeding those resulting from similar oral doses of other antibiotics
- ★ Produces a first-class therapeutic response

Serum concentration of Biotexin following oral administration



BIOTEXIN TRADE MARK *Tablets: 125 mg. of novobiocin sodium. Bottles of 32 and 100*

GLAXO LABORATORIES LTD., GREENFORD, MIDDLESEX BYRon 3434

Subsidiary Companies and Agents in most Countries

INVOLVEMENT OF THE NERVOUS SYSTEM IN BEHÇET'S SYNDROME

REPORT OF THREE CASES AND ISOLATION OF VIRUS

A. D. EVANS
M.B., B.Sc. Wales, Dip. Bact.
SENIOR BACTERIOLOGIST, PUBLIC HEALTH LABORATORY, CARDIFF

C. A. PALLIS
M.A., D.M. Oxfd, M.R.C.P.
SENIOR NEUROLOGICAL REGISTRAR, CARDIFF ROYAL INFIRMARY

J. D. SPILLANE
M.D., B.Sc. Wales, F.R.C.P.
NEUROLOGIST, UNITED CARDIFF HOSPITALS

WE report here the clinical features of three cases of Behçet's syndrome with involvement of the nervous system. A virus was isolated from the eye and brain of one of the two patients who died of the disease. Some observations on the titre of virus-neutralising antibody in the sera of eleven patients with Behçet's syndrome are described, together with parallel observations on the sera of healthy controls.

Behçet's syndrome (Behçet 1937, 1938, 1939, 1940) is characterised by relapsing iritis and recurrent ulceration in the mouth and on the genitalia. Less common findings include thrombophlebitis, various types of rash (erythema nodosum, acne, furunculosis), arthralgia with or without hydrarthrosis, and ocular disorders such as keratitis, conjunctivitis, and hæmorrhages into the retina or the vitreous. The nervous system may occasionally be affected (Knapp 1941, Berlin 1944, Alm and Öberg 1945, Gray 1950, Magni 1951, Silfverskiöld 1951, Phillips and Scott 1955, Pallis and Fudge 1956), the prognosis then being extremely grave. Of the thirteen patients with such neurological complications reported up to the end of 1956 at least six have died of the disease. It is particularly noteworthy that Behçet's syndrome has hitherto been fatal only when the nervous system has been involved.

Evidence that Behçet's syndrome may be due to a virus, which occasionally exhibits neurotropic tendencies, has recently been accumulating.

Behçet originally claimed to have found inclusion bodies in smears of hypopyon fluid and of exudate from the ulcers in the mouth. Jensen (1941) could not confirm this finding.

Alm and Öberg (1945) injected cerebrospinal fluid (C.S.F.) from their patients into rabbits by the cisternal route. The rabbits developed focal encephalitis, optic neuritis, uveitis, keratitis bullosa, and conjunctivitis.

Katzenellenbogen (1946) inoculated material from oral and genital ulcers in a case of Behçet's syndrome on to the cornea of a rabbit and intracerebrally into mice, but no infection resulted.

Curth (1946) prepared suspensions of oral and genital scrapings in isotonic saline solution and inoculated them into mice, guineapigs, and cotton-rats (routes not given) and on to embryonated hen's eggs and chick-embryo tissue-cultures of the Li-Rivers type, but no virus grew.

Sezer (1953) was the first to claim isolation of the virus responsible for Behçet's disease. Fluid obtained from the vitreous of an enucleated eye and "subretinal" serous fluid obtained by puncture in two other patients were inoculated into the chorio-allantoic membranes of fertile eggs and into allantoic fluid and yielded a growth of virus. After several passages the material was injected intracerebrally into mice (causing encephalitis), into the vitreous of rabbits (causing chorioretinitis and hypopyon), and either intraperitoneally or subcutaneously into guineapigs (causing fatal hæmorrhagic pneumonia). Sezer also claims that this material gave strongly positive complement-fixation and neutralisation reactions with the sera of twelve patients with Behçet's syndrome but not with normal sera. He maintains that the failure of his predecessors was due to "the limitation of their investigations to the fluid of the anterior chamber and the exudate of the aphthæ" and that "the pathological agent of the disease apparently resides in the posterior segment of the eye and is probably absent from the mouth and genital organs as well as from the hypopyon." Sezer (1956) later claimed to have isolated the virus from both blood and urine in twenty patients in the active "ulcerating" phase of the illness, and to have found, at various times, a high titre of complement-fixing antibody in the sera of these patients. He claims that intermittent viræmia characterised the disorder, and that there was an inverse relationship between the degree of this viræmia and the titre of complement-fixing antibody. Sezer's findings have not hitherto been confirmed.

The histological changes in the nervous system in fatal cases of Behçet's disease have not yet been fully studied. Necropsy findings have only been published in three such cases (Berlin 1944, Magni 1951, Silfverskiöld 1951) and contribute but little to the question of ætiology.

Case-reports

Partial accounts of cases 1 and 2 have already been published (Pallis and Fudge 1956). Both patients have since died. The following reports include details of the later stages of their illnesses.

FIRST CASE

Man, aged 47. Recurrent iritis (bilateral) for 4 years; keratitis; recurrent ulceration of genitalia, legs, and forearms for 10 months; spastic paraplegia of sudden onset; flexor spasms; retention of urine. Cystostomy. C.S.F. forming gel (protein 5200 mg. per 100 ml.). Myelographic features of arachnoiditis. Plasma fibrinogen 700 mg. per 100 ml.

A miner, he had attended the ophthalmic department of Cardiff Royal Infirmary in 1949 for right-sided iritis and had later developed left-sided iritis followed by keratitis. In April, 1953, painless ulcers appeared on the glans penis and scrotum: they recurred at intervals of a few weeks and healed slowly. Later, ulcers developed on his knees, shins, and the extensor surfaces of his forearms. He had not had any ulcers in his mouth.

In June, 1953, he had low backache and slight difficulty in initiating micturition.

First Admission

When admitted to Bridgend Hospital on Sept. 30, 1953, for biopsy of a penile ulcer, he was ambulant and there were no abnormal neurological signs. Repeated Wassermann and Kahn tests were negative (in two different laboratories). His C.S.F. was rather surprisingly found to contain protein 510 mg. per 100 ml. The C.S.F. clotted rapidly, making an accurate cell-count impossible. Lange test 1555333320. Wassermann reaction negative. During a three-month stay in hospital he received injections of penicillin, bismuth, and neoarsphenamine. Several new penile sores appeared during this period. A diagnosis of Behçet's syndrome was first suggested by Dr. F. L. Dyson.

Shortly after the patient's return home, severe weakness of both lower limbs developed within a period of a few hours, the feet became "ice-cold," and numbness ascended to waist level. He had difficulty in voiding urine. Flexor spasms occurred.

Readmission

He was readmitted to Bridgend Hospital with complete retention of urine. Suprapubic cystostomy was performed, and he was transferred on Feb. 17, 1954, to the neurological department of Cardiff Royal Infirmary.

At this time he looked ill, being pale, thin, and febrile, with sacral bedsores. He had ulcers on the glans penis, scrotum, and right knee, above the right external malleolus, on the anterior aspect of the right thigh, and on the extensor surface of the right forearm. An almost healed ulcer was seen on his palate. He had small areas of dry gangrene under several finger-nails. His epitrochlear glands were palpable, and firm enlarged nodes were felt in both axillæ and both groins. His liver was slightly enlarged.

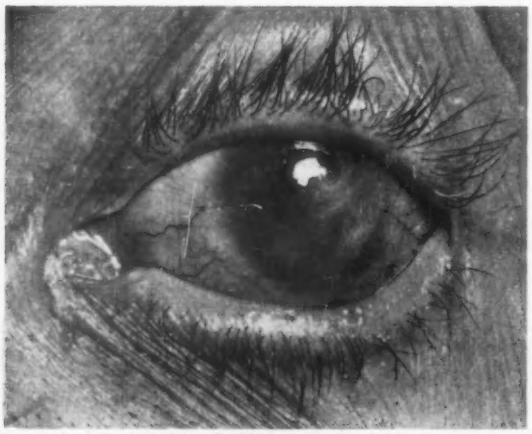


Fig. 1—Case 1: keratitis. Residua of previous iritis can be seen in irregularity of medial border of pupil.

Visual acuity was 6/12 on the right, but on the left, where there had been previous keratitis (fig. 1), it was reduced to counting fingers at 1 metre. The right fundus appeared normal. No abnormal neurological signs were found in the upper limbs. Both legs were weak, and he could only just raise them off the bed. He had sustained patellar and ankle clonus and extensor plantar responses. His lower abdominal muscles were weak, the abdominal reflexes being absent in the lower quadrants but retained in the upper. All modalities of sensation were depressed below T10, the loss being maximal, bilaterally, from T11 to L2. There was a suggestion of "sacral sparing." He was constipated but could void urine per urethram.

Investigations

Hæmoglobin 11·6 g. per 100 ml.; red cells 4,500,000 per c.mm.; leucocytes 9600 per c.mm. (differential count normal); erythrocyte-sedimentation rate (E.S.R.) 35 mm. in 1 hour (Wintrobe); blood-urea 32 mg. per 100 ml.; Wassermann and Kahn tests negative; total plasma-proteins 6·7 g. per 100 ml. (albumin 3·2 g. per 100 ml., globulin 2·8 g. per 100 ml., fibrinogen 700 mg. per 100 ml.). Urine: 20–30 pus cells per high-power field. Culture yielded *Escherichia coli*.

Radiographs did not show any periosteal reaction under the various sites of cutaneous ulceration. There was erosion of the terminal phalanges in those fingers in which small areas of dry gangrene had appeared under the nails.

C.S.F. was obtainable from the lumbar theca only by aspiration; it was turbid, and clotted within four minutes, forming a grey gel. A further sample collected in citrate contained total protein 5200 mg. per 100 ml. (albumin 2300 mg. per 100 ml., globulin 2500 mg. per 100 ml., fibrinogen 400 mg. per 100 ml.). The specimen contained a few cells, but an accurate count was impossible. The protein content of cisternal C.S.F. was only 70 mg. per 100 ml., and this fluid contained less than 5 cells per c.mm. Lange 4444322110. Wassermann negative. In view of the striking difference in protein content of the two samples and of the definite sensory level, cisternal myelography was performed. The streaky pattern and behaviour of the ethyl iodophenylundecylate ('Myodil') on screening suggested that adhesions narrowed the subarachnoid space over a large area in the spinal canal in the lower thoracic and lumbar regions.

Treatment and Progress

The patient received 200 mg. of cortisone daily for 5 days, followed by 100 mg. daily for 10 days, without apparent improvement. A fresh ulcer developed on his leg during this period.

The weakness of his lower limbs fluctuated slightly over the next few weeks, but his general condition deteriorated steadily. At no stage was there any disability in his upper limbs or did any symptoms develop referable to the brain-stem. He developed bedsores and a urinary infection which did not respond to treatment, became cachectic, and died at home, presumably of pyelonephritis, in July, 1954, about a year after the development of the first neurological symptoms. Necropsy was not performed.

SECOND CASE

Man, aged 44. Recurrent ulceration of mouth and genitalia, 15 years; progressive stiffness of right arm and both legs, 18 months. Intellectual deterioration; parkinsonian features; pathological laughter and crying; dysarthria; spastic tetraparesis with predominant rigidity; nystagmus; gaze pareses; jaw clonus. C.S.F. protein 90 mg. per 100 ml., 6 cells per c.mm. (50% polymorphs). Plasma fibrinogen 800 mg. per 100 ml.

A miner, he was admitted to the neurological department of Cardiff Royal Infirmary on March 4, 1955. He had had painful crops of ulcers in his mouth and on his scrotum for about 15 years. At first two or three lesions would develop simultaneously, but lately outbreaks often consisted of as many as a dozen ulcers, which would take 2–3 weeks to heal. He had had to give up work in 1953 because soreness in the perineum had prevented him from getting about. Over a period of 18 months his right arm had become increasingly stiff and awkward, and walking had become slow and shuffling. He had not experienced any pain in his limbs. Some mental deterioration had been noticed, and for about a year he had been liable to outbursts of unwarranted laughter and weeping. Control of his sphincters had not been affected. No history of iritis. No family history of neurological disorder.

Examination

He was well covered and of good colour, with a fatuous, rather expressionless, greasy face. He had little insight, was euphoric and mildly catatonic, and his speech was slow and stiff. He cerebrated slowly. Pathological laughter and weeping could easily be elicited. A shallow ulcer was seen at the angle of the mouth, on the right side, and there was some scarring about the palate. A whole crop of recent ulcers were scattered on the posterior surface of his scrotum (fig. 2), which also showed considerable scarring. His trunk and arms showed slight acne. There was no adenopathy, and no abdominal viscera were palpable.

The optic discs were rather pale and their edges unusually sharp. Corrected visual acuity was 6/12 R.E. and 6/9 L.E. Conjugate gaze was poorly maintained laterally, and conjugate upward gaze was defective. A sustained "jelly-like" nystagmus developed when he tried to look up and was also present on looking to the right. Coarse nystagmus was obvious on looking to the left. His jaw-jerk was very brisk, with clonus at times. His face was spastic. No reflex pouting or sucking. Repetitive tongue movements were laboriously performed, although there was no obvious weakness. There was increased tone in the flexors of his neck and rigidity in all the muscle groups of his right arm and both legs (especially the right), with moderate adductor hypertonus of both thighs and bilateral spastic foot-drop with contractures. No tremor. Power was slightly reduced in the affected limbs, but most of the disability appeared to be due to rigidity rather than paresis. There was pronounced bradykinesia. His gait was awkward and stiff, but he could get about the ward unaided. No cerebellar signs were found in his unaffected left arm. He was a poor sensory witness, but there were no obvious abnorm-

Fig. 2—Case 2: recent crop of scrotal ulcers typical of lesions of Behçet's syndrome.

alities. The reflexes were pathologically brisk in both arms, with slight extensor clonus at the right wrist. His abdominal reflexes were absent, knee-jerks brisk, ankle-jerks rather sluggish, and both plantar responses extensor.

Investigations

Hæmoglobin 14·8 g. per 100 ml. (100%); normal white-cell and differential counts. E.S.R. 17 mm. in 1 hour (Wintrobe). Blood-urea 46 mg. per 100 ml., Wassermann and Kahn tests negative. Clotting-time (Dale and Laidlaw) 12 minutes (normal 5–12 minutes). Bleeding-time (Duke) 3 minutes. Total plasma-protein 7–5 g. per 100 ml. (albumin 4·3 g. per 100 ml., globulin 2·7 g. per 100 ml., fibrinogen 500 mg. per 100 ml.). The electrophoretic pattern was normal. Several direct estimations of the plasma-fibrinogen were made, the readings varying from 200 to 800 mg. per 100 ml.; the highest value was recorded within 3 days of the outbreak of a fresh crop of ulcers. Liver-function tests normal. C.S.F., protein 90 mg. per 100 ml.; Pandy positive; Lange 1111100000; Wassermann negative; cells 6 per c.mm. (50% polymorphs).

Radiographs of the skull were normal. Films of the chest showed pneumoconiotic nodulation.

Treatment and Progress

Benzhexol hydrochloride at first slightly lessened his rigidity and was taken continuously for several months. Cortisone 100 mg. daily was given for 3 weeks, but ulcers continued to develop. Courses of oxytetracycline, aureomycin, and erythromycin had no effect on the severe recurrent orogenital ulceration. The neurological disorder progressed without intermission, the rigidity and tetraparesis becoming extreme and gradually preventing the patient from walking and from feeding himself. His speech became unintelligible and swallowing very difficult. Spastic laughter and weeping became pronounced. No visual symptoms developed.

He was admitted to another hospital on Dec. 16, 1955, and died of bronchopneumonia on Dec. 28, 1955, about 2 years after the appearance of the first neurological symptoms.

Necropsy

A partial necropsy was done within 3 hours of death. In view of the subsequent isolation of a virus from the eye and nervous system of this patient (and of the fact that some doubt exists about the precise source of the infective material) the technique used is reported in detail.

The eyes were left in situ. A large-bore needle was inserted into the right eyeball at the 3 o'clock point, just lateral to the limbus, and an attempt was made to aspirate vitreous. Suction was exerted, but no material entered the syringe. It is not excluded that vitreous contents may have contaminated the lumen of the needle. The same needle, unfortunately, was then used in an attempt to obtain aqueous. About 1 ml. of fluid was readily obtained from the anterior chamber of the right eye. The material was stored for several days in the "deep-freeze" before being conveyed, in ice, to the Public Health Laboratory, Cardiff.

The calvarium and underlying dura were then removed and the cerebral hemispheres slightly separated (with the brain in situ). A wide-bore needle was inserted in the midline, in a downward and caudal direction, through the most anterior part of the corpus callosum, into the third ventricle. 2 ml. of C.S.F. was readily obtained, together with a small fragment of tissue (about $2 \times 1 \times 1$ mm.), possibly from the posterior part of the floor of the third ventricle but more probably from the corpus callosum itself. This material was also stored in ice for several days before being sent to Cardiff.

Histology

The brain and spinal cord were then removed and fixed in 10% formol-saline solution. They presented no macroscopic abnormalities. The histological findings are described in detail by McMenemey (1957). In brief they consisted of (1) small focal softenings in both grey and white matter, largely confined to the mid-brain, pons, and medulla, with occasional small areas of perivascular demyelination, and (2) perivascular cuffing, most obvious in the brain-stem but also apparent in the insula and spinal cord. These were mainly related to veins. Nerve-cell changes were only slight. No inclusion bodies were found. No primary thrombi were seen.

THIRD CASE

Woman, aged 22. Recurrent oral ulceration for 7 years. Vulval ulceration, 5 years. Furunculosis. Intermittent blurring of vision and weakness of right leg for 2 years. Bilateral vitreous haze. Variable bilateral central scotomata. Attacks of conjunctivitis. Single attack mild iritis. Intermittent pyrexia. Pleocytosis in C.S.F. without clinical evidence of meningitis. Virus-neutralising antibody titre 1/128.

An unmarried woman, she had had recurrent superficial ulceration of the tongue, fauces, and buccal mucosa for 7 years and attacks of vulval ulceration, usually premenstrual, for 5 years. Each bout of ulceration lasted about 2 months. For 2 years she had repeated attacks of blurring of vision, affecting one or other eye, lasting several weeks at a time and sometimes associated with mild retro-ocular pain. The vision would improve substantially but never quite return to normal between the attacks. For about 2 years she had noticed mild periodic heaviness of her right leg, but this had not troubled her in the weeks preceding admission.

First Admission

On admission to the neurological department of Cardiff Royal Infirmary on Aug. 18, 1956, she had furunculosis of her nares and right external auditory canal and scarring from recent ulceration on her palate and the right side of her tongue. There was no adenopathy. No abdominal viscera were palpable. She had slight tachycardia (90–100) and blood-pressure 130/70 mm. Hg. Externally her eyes appeared normal. Visual acuity in the right eye was 5/60, in the left eye 6/18. There was a faint vitreous haze on each side. There was a "macular star" on the right. Her right disc appeared normal, and no hæmorrhages were seen. Just above her left disc a silvery-white streak, about 2 disc diameters in length, was noted, resembling retinitis proliferans. The field of her right eye showed a central scotoma extending about 8° from the fixation point, in all directions. Her pupils were equal and circular. Her right pupil reacted sluggishly to direct light. The consensual reaction was brisk. There was no nystagmus and no abnormal motor, sensory, or reflex signs in her limbs. Her oral temperature reached 99°F on several occasions.

She was given a 4-week course of cortisone 50 mg. t.d.s. in the first week and 25 mg. t.d.s. in the second and subsequent weeks. The slight pyrexia subsided, but there was no improvement in the visual acuity.

Readmission

She was readmitted three months later, on Dec. 8, 1956. Recurrent oral and genital ulceration had persisted. Since her discharge she had had three attacks of conjunctivitis associated with photophobia. Her general health had remained good. During an attendance as an outpatient her left pupil was noted to be widely dilated and grossly irregular, from posterior synechiæ. On admission to hospital a few days later these had ruptured and the pupils were equal again.

The visual acuity in the right eye had deteriorated to 3/60 and in the left eye was now reduced to counting fingers at 1 metre. The right vitreous haze persisted, but the macular exudate had been resorbed. There was slight pallor of the disc. In the left eye there was a definite aqueous flare (by lens and loupe), and pigment masses were seen on the anterior surface of the lens. The left fundus appeared normal, apart from the previously noted fibrous streak. Visual acuity was obviously more grossly impaired than could be explained by the changes in the media, and scotometry revealed bilateral central scotomata. The pupils were of normal size and reacted to light rather sluggishly. There were again no abnormal neurological signs.

There was gross œdema of the labia minora, with several superficial ulcers and moderate inguinal adenopathy. Although there was no constitutional disturbance the patient had pyrexia up to 101°F. Her pulse-rate was very variable, fluctuating between 70 and 120. She was kept in hospital for 6 weeks, during which she had a second course of cortisone (50 mg. t.d.s. for 4 weeks). Her pyrexia subsided. By Jan. 19, 1957, the visual acuity in her right eye had improved to 6/36 and in her left to 6/18. Further examinations on the Bjerrum screen showed considerable diminution in the size of both central scotomata.

Investigations

Radiographs of skull, sinuses, and chest were normal. E.S.R. (Wintrobe) 12 mm. in 1 hr. (Aug. 20, 1956) and 20 mm. in 1 hr. (Nov. 30). Wassermann reaction and Kahn test negative on both occasions. Hb 14·4 g. per 100 ml. (97%). Total white counts showed a variable slight neutrophil leucocytosis, which subsided when the secondary infection of the vulval ulcers was brought under control. Serum-total protein 6·7 g. per 100 ml., serum-albumin 3·7 g. per 100 ml. (Howe), plasma-fibrinogen (direct estimation) 400 mg. per 100 ml. A swab from the right ear yielded a heavy growth of coagulase-

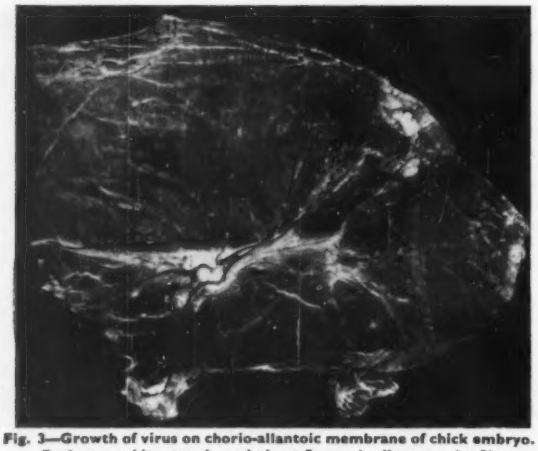


Fig. 3—Growth of virus on chorio-allantoic membrane of chick embryo. Pocks are white, tough, and about 5 mm. in diameter (× 2).

negative *Staphylococcus albus*. On Dec. 17, 1956, a lumbar puncture was done when the patient had no headache and no clinical signs of meningitis. The C.S.F. contained 33 lymphocytes per c.mm.; protein 36 mg. per 100 ml.; sugar 45 mg. per 100 ml.; and chloride 440 mg. per 100 ml. A further sample was collected on Jan. 7, 1957; the cell-count had fallen to 2 per c.mm. and the sugar had increased to 58 mg. per 100 ml.

On Jan. 18 Sir Tudor Thomas obtained for culture a little fluid from the anterior chamber of the left eye. The chorio-allantoic membranes of fertile hen's eggs were inoculated with (1) blood, (2) urine, (3) C.S.F. (on two occasions), and (4) aqueous fluid, but attempts to isolate virus from those sources failed. The samples of urine and blood had been collected during a phase of active oral and genital ulceration.

The titre of virus-neutralising antibody was estimated on three occasions (both in active and relatively quiescent phases of the illness); a titre of 1 : 128 was obtained on each occasion.

Isolation of Virus from Case 2

Approximately 0·2 ml. of undiluted "aqueous," obtained as described, was inoculated on to the chorio-allantoic membrane of each of fifteen fertile 10-day-old hen's eggs.

The specimen of brain tissue was homogenised and diluted to make a 10% suspension in sterile distilled water. This suspension was inoculated in 0·2-ml. amounts on to fifteen further eggs.

After 4 days' incubation at 35°C half the eggs were chilled and examined. Intense congestion of the chorio-allantois and scanty pock formation were seen in one of the eggs inoculated with "aqueous" and in two of those inoculated with brain suspension. The pocks were 5 mm. in diameter (fig. 3), tough, and white. An occasional vesicle was seen in the centre. The pocks tended to break down and become necrotic. By the 6th day of incubation death of the embryo (as well as congestion and pock formation on the chorio-allantois) had taken place in two further eggs inoculated with brain suspension.

It was possible to establish the strain by passage of ground-up infected chorio-allantoic membranes. After 21 such passages the virus can now be transmitted at a titre of 10^{-4}. The congestion and pock formation are apparent by the 2nd day after inoculation, but death of the embryo is not a constant feature, occurring in just under half the cases, usually on the 5th day.

The agent will pass a Seitz E.K. pad filter. Repeated attempts to adapt it to cultures of human embryo kidney cells, human amnion cells, and HeLa cells have been unsuccessful. Attempts to transmit the agent to mice, guineapigs, and rabbits by the intracerebral intramuscular, and intraperitoneal routes have also failed.

The infective agent for the chorio-allantois was not neutralised by hyperimmune serum to such pock-producing organisms as herpes febrilis and vaccinia virus.

Neutralisation Tests

Through the coöperation of the dermatological, ophthalmic, and neurological departments at St. Bartholomew's Hospital, the London Hospital, the Leeds General Infirmary, Addenbrooke's Hospital, Cambridge, and the Radcliffe Infirmary, Oxford, sera were obtained from eleven patients considered to have Behçet's disease. As the mucocutaneous lesions may precede the ocular ones by several years, we have accepted Curth's (1946) suggestion that a diagnosis of Behçet's disease is justifiable when two of the three main features (oral, genital, and ocular lesions) are well in evidence. Six of the patients had the fully developed syndrome (in three of these cases the nervous system was also affected). The remaining five patients had severe oral and genital ulceration only.

The sera, in each case, were collected during active "ulcerating" phases of the illness, most of the patients only attending their respective clinics at such times. If Sezer's (1956) claims are correct, this timing of the sampling would yield the lowest titre of virus-neutralising antibody. Serial readings were obtained in some of the patients, and in such instances we have only recorded the lowest titre obtained. Our findings relate to the minimum virus-neutralising titres in patients with Behçet's disease. The significance of raised titres is enhanced in these circumstances.

Serial doubling dilutions of inactivated serum were incubated at 37°C for 1 hour with chorio-allantoic membrane suspension diluted to contain 25 ID 50 (judged by pock formation). 0·2 ml. of the mixture was inoculated into four eggs for each dilution. The results were read after 3 days' incubation at 35°C.

A 50% end-point was calculated by the Reed and Muench (1938) method. The accompanying table shows

TITRE OF VIRUS-NEUTRALISING ANTIBODY IN ELEVEN PATIENTS WITH BEHÇET'S SYNDROME

No.	Sex	Age (yr.)	Titre	Oral	Genital	Ocular	Neurological
1	F	34	1/2	+	+	+	0
2	F	22	1/128	+	+	0	0
3	F	13	<1/2	+	+	0	0
4	F	16	<1/2	+	+	0	0
5	F	27	1/128	+	+	0	0
6	M	40	1/32	+	+	+	+
7	F	24	1/64	+	+	0	0
8	F	33	1/2	+	+	+	0
9	F	17	1/16	+	+	+	0
10	F	21	1/128	+	+	+	+
11	F	30	1/64	+	+	+	+

the main clinical features and the antibody titres in these cases. It will be seen that six of the eleven patients showed a titre of virus-neutralising antibody of $^1/_{32}$ or more. All three patients with involvement of the nervous system had a significantly raised titre of virus-neutralising antibody. These include patient A. D. (case 2 of Wadia and Williams 1957) who had a virus-neutralising antibody titre of 1/32.

The sera of fourteen persons who had never had oral or genital ulceration or iritis were also examined. There were eight males and six females in this group, all volunteers, attending the Regional Blood Transfusion Service, and ranging in age from 19 to 61. None of these sera contained a detectable amount of neutralising antibody.

Comment

In its more usual manifestations Behçet's syndrome, although at times painful, is relatively benign. The long-term effects on vision may be crippling, but the patient's life is not in danger. The prognosis changes completely

in the small minority of cases where the nervous system is affected. The condition has proved fatal in nearly half of such cases.

Much remains to be explained in relation to the pathology. There is a discrepancy between the serious outcome in those cases with involvement of the nervous system and the paucity of demonstrable neuropathological findings. Although these are probably compatible with a virus ætiology they are not characteristically those of a polioclastic infection. The isolation of a virus from a case with such non-specific pathological features may possibly have important implications in relation to other chronic or relapsing disorders of the nervous system. Moreover it probably justifies the use of the term Behçet's disease rather than Behçet's syndrome.

Our thanks are due to Dr. B. J. Fudge for his follow-up of case 2 after discharge from hospital and for his assistance in obtaining permission for the necropsy; Dr. John B. Raffan, of Bridgend Hospital, who performed the necropsy and obtained the specimens for us; and Mr. Ralph Marshall for two of the photographs.

REFERENCES

Alm, L., Öberg, L. (1945) *Nord. Med.* **25**, 603.
Behçet, H. (1937) *Derm. Wschr.* **105**, 1152.
— (1938) *Bull. Soc. franç. Derm. Syph.* **45**, 420.
— (1939) *Ibid*, **46**, 674.
— (1940) *Dermatologica, Basel*, **81**, 73.
Berlin, C. (1944) *Arch. Derm. Syph., N.Y.* **49**, 227.
Curth, H. O. (1946) *Ibid*, **54**, 179.
Gray, G. S. (1950) *Canad. med. Ass. J.* **62**, 597.
Jensen, T. (1941) *Acta derm.-venereol., Stockh.* **22**, 64.
Katzenellenbogen, I. (1946) *Brit. J. Derm.* **58**, 161.
Knapp, P. (1941) *Schweiz. med. Wschr.* **71**, 1288.
McMenemey, W. H., Lawrence, B. J. (1957) *Lancet*, ii, 353.
Magni, S. (1951) *Riv. oto-neuro-oftal.* **26**, 445.
Pallis, C. A., Fudge, B. J. (1956) *Arch. Neurol. Psychiat., Chicago*, **75**, 1.
Phillips, D. L., Scott, J. S. (1955) *Lancet*, i, 366.
Reed, L. J., Muench, H. (1938) *Amer. J. Hyg.* **27**, 493.
Sezer, F. N. (1953) *Amer. J. Ophthal.* **36**, 301.
— (1956) *Ibid*, **41**, 41.
Silfverskiöld, B. P. (1951) *Acta psychiat. neurol. scand.* **26**, 443.
Wadia, N., Williams, E. (1957) *Brain*, **80**, 59.

ENCEPHALOMYELOPATHY IN BEHÇET'S DISEASE

REPORT OF NECROPSY FINDINGS IN TWO CASES

W. H. McMENEMEY
M.A., D.M. Oxfd, F.R.C.P., D.P.M.
PATHOLOGIST, MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, LONDON

BERYL J. LAWRENCE
M.B. N.Z., D.C.H., D.P.H., D.C.P.
PATHOLOGIST, REPATRIATION HOSPITAL, HOLLYWOOD, W. AUSTRALIA

NEUROLOGICAL complications of Behçet's disease are uncommon but carry a serious threat to life.

Pallis and Fudge (1956) review the findings in thirteen cases, and divide them into a brain-stem syndrome, episodic or irregularly progressive; a meningomyelitic type, with fever; and a cerebral disorder characterised by confusion. The first seems to be the most common but any combination of them is possible. Wadia and Williams (1957) have reported three more cases and Curth (1952) another. Others are under observation (Critchley 1957).

Of the seventeen reported cases, death has already occurred in six: necropsies have been reported on three of them (Berlin 1944; Silfverskiold 1951, case 2; Magni 1951 and Alema and Magni 1952).

We now present our findings in two others. The clinical history of the second has already been recorded by Pallis and Fudge (1956, case 2) and Evans, Pallis, and Spillane (1957, case 2).

Case-reports

THE FIRST CASE

Clinical Findings

A native of Perth, W. Australia, was a despatch hand in a firm of clothiers and household furnishers. He enlisted in the army at the age of 21, and within a year recurrent and refractory conjunctivitis developed with corneal ulceration and iritis, followed by synovitis of an ankle and pain in the soles of his feet. He returned to his former occupation but had to abandon it at the age of 26 because of his eye disease. In the following year he had "shingles" of the right side of his trunk and arm, and "ulcers" in his mouth which rapidly worsened. The "shingles" later spread to the right side of his forehead, but the eye disease was now quiescent. He had cervical adenitis. Within a month the rash had gone and his mouth was better. A few months later his right eye became inflamed and painful and this condition recurred over a period of 18 months.

He was now in the 6th year of his disease. His left eye showed diffuse corneal nebulæ and extensive posterior synechia from the previous attacks of iritis. About a month later he complained of pain over the left eye and had three fits within 90 minutes. These were followed by many others at varying intervals. There were no neurological signs at this time. The left fundus oculi could not be seen but the right was normal. The pitting and scarring of the right forehead was thought to be compatible with previous herpes zoster but a few small pustules and papules were to be seen on one arm, and there were ulcers on the tongue. A diagnosis of Behçet's disease was made, but no history of genital ulceration could be obtained.

In the next year, after a series of fits, a left hemiparesis developed. Lumbar puncture yielded a clear fluid under a pressure of 210 mm., no cells, total protein 110 mg. per 100 ml., Lange 0112332210. All tests for syphilis were negative. A slight improvement followed, and for a while he was treated with "smallpox vaccine," and later with diphenhydramine and then antazoline. He left hospital, but after a few months the disease relapsed again and he was readmitted for the last time. There was a generalised eruption resembling erythema multiforme. The fits became more and more frequent. Contractures developed in both legs and the left arm, and he died of respiratory infection on Nov. 24, 1948, at the age of 29.

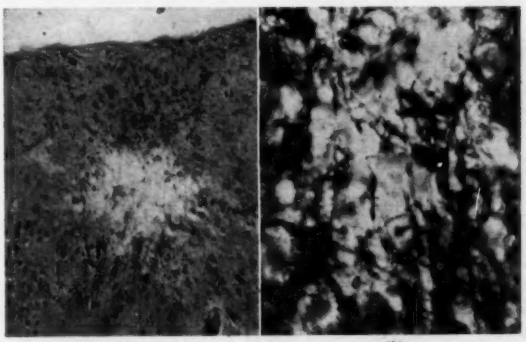
Necropsy

This was performed by one of us (B. J. L.) within 6 hours of death. He had many small areas of pigmentation in the skin of limbs and trunk. The tongue was smooth anteriorly and devoid of papillæ in parts; there was a small shallow ulcer on the anterior edge. Posterior to the circumvallate papillæ, there were many fibrous papillæ or tags, which were present in smaller numbers in the pharynx and in the pyriform fossa.

The brain (after fixation).—The leptomeninges over the vertex were whitened. The left inferior temporal gyrus and upper and outer part of left occipital lobe were soft and thin. The white matter of the left temporal lobe, especially the inferior temporal gyrus, was shrunken. There was no general atrophy of white matter: ventricles not dilated.

Histology

Cerebrum.—Both cortex and white matter, including the corpus callosum, contained innumerable small softenings (figs. 1 and 2), especially near the corticomedullary junction. They were equally plentiful in the frontal and occipital lobes and cornu Ammonis but less so in the temporal lobe. In the



(a) (b)

Fig. 1—Case 1. Focal softenings in right superior frontal gyrus, showing: (a) Mild astroglial reaction (paraffin, hæmatoxylin, and eosin; ×70); (b) Thinning of axons with nodular swellings (paraffin, Glees's silver impregnation; ×280).

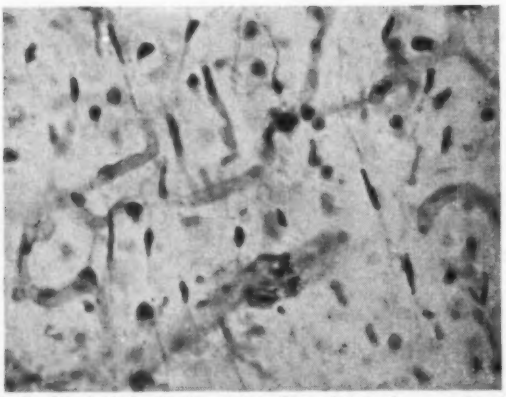


Fig. 2—Case I. Left calcarine cortex. There is loss of nerve-cells with marked microglial activity and formation of "rod" cells (frozen—Cone-Penfield's silver impregnation; ×280).

occipital lobes there was a greater tendency to involvement of white matter, with many minute spongy areas in addition to the softenings: this was accompanied by a swelling of the oligodendroglia and an increase in the number of astrocytes, many of which were hypertrophic. A number of the arterioles and venules were cuffed by hæmosiderin-filled macrophages and sometimes small mononuclear cells. The striate cortex showed a general loss of cells with many "rod" cells and proliferating astrocytes. In the cortex adjacent to the parieto-occipital fissure there was a more advanced state of ischæmic necrosis: nerve-cell loss here was considerable and was associated with a fibrillary gliosis through which coursed many blood-vessels cuffed with compound granular corpuscles: in the upper laminæ of the cortex there was a marked overgrowth of gemästete astrocytes. The softenings contained fat-laden compound granular corpuscles and swollen astrocytes, sometimes binucleated, while the surrounding astrocytes showed moderate proliferation but only slight fibre-formation. Often they were related to distended capillaries or venules and were sometimes confluent: no thrombi were seen. Some nerve-cells in the immediate vicinity showed degenerative changes, but others did not. The left inferior temporal gyrus was devastated, but a few areas of relative preservation were found in the deeper laminæ. In the atrophied parts, the loss of nerve-cells was complete and was accompanied by proliferation of fibre-forming astrocytes giving a spongy appearance: ferruginised nerve-cells were identified in the lower laminæ in the depths of a sulcus. In the white matter deep to this ischæmic gyrus there was evident loss of myelin with swollen astrocytes, calcified capillaries (sometimes invested by hæmosiderin-filled histiocytes) and laminated calcified bodies from 7 to 12 μ in diameter. In the cornu Ammonis there was a general loss of nerve-cells, especially in Sommer's sector, with much microglial and astroglial activity.

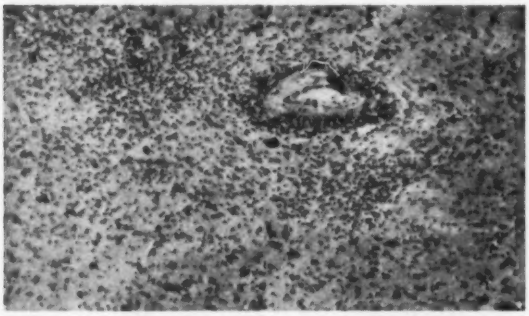


Fig. 3—Case I. Infarcted area in left putamen. The investing cells are mostly lymphocytes and histiocytes. There is a loss of nerve-cells with an increase in microglia and astrocytes (celloidin, hæmatoxylin, and eosin; ×70).

Basal ganglia.—Softenings were present throughout these centres, with extensive infarction in the putamen where there were solitary instances of both endarteritis and of post-thrombotic recanalisation (fig. 3). A loss of neurones, with an excess of lipochrome in the survivors and an increase in astrocytes, was noted in both the caudate nucleus and putamen, and there was siderosis of the globus pallidus.

Softenings were present in the anterior and posterior commissures, the fornix, and the commissures of Meynert and particularly in the optic tracts and external and internal capsules (fig. 4). They were present also in the nucleus ruber, corpora Luysii, the medial and lateral geniculate bodies and corpora mammillaria. There was a general increase of microglia in the thalamus and claustrum.

Brain-stem.—There was a long-standing pyramidal-tract degeneration on the right, with small areas of softening in both crura and inferior colliculi and decussation of brachia conjunctiva. They were often in relation to capillaries. The cells of the substantia nigra appeared normal. *Pons:* About ten minute foci of degeneration, showing, if anything, a preference for the white matter: one or two were larger and a study of their outline suggested the possibility of their being the result of a confluence of two or more of the smaller ones. *Medulla:* Only a few lesions and all minute. *Cerebellum:* No significant changes, except for a few minute foci of microglial activity in white matter.

Spinal cord.—Pyramidal-tract degeneration, bilateral in the lumbar region but more marked on the left in the cervical cord. Some posterior-column degeneration throughout. In the demyelinated areas of the cervical cord, fat-laden histiocytes surrounded the vessels, some of which also showed a slight cuffing of lymphocytes. Small compact thrombus in venule in pia-arachnoid, but otherwise no suggestion of vascular

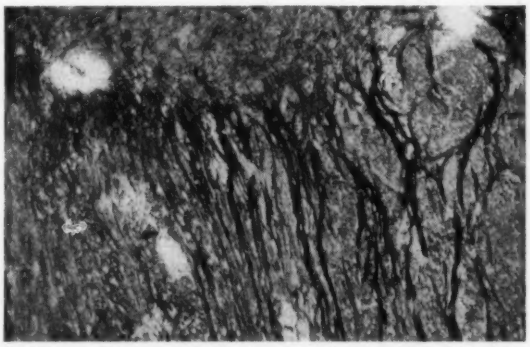


Fig. 4—Case I. Numerous softenings at medial edge of lenticulothalamic part of right internal capsule (celloidin, Heidenhain; ×26).

obstruction. The anterior-horn cells were present in normal numbers, only a few showing minor departures from normal. A few areas of necrosis, mostly in the grey matter—one of them hæmorrhagic and recent.

Eyes.—There was chronic iridocyclitis of the left eye with much destruction of tissue; the optic nerve was atrophied with no sign of inflammation.

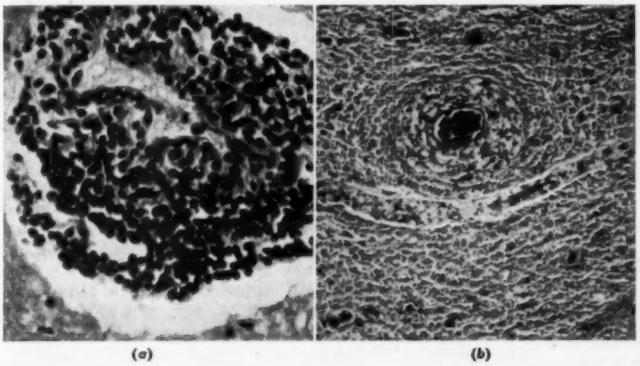
Other organs.—No naked-eye or microscopic lesion, except for basal congestion of the lungs and myocardial degeneration.

THE SECOND CASE

Clinical Summary

A man, aged 44, had had recurrent ulceration of the mouth and genitalia for 15 years. Increasing stiffness of the right arm, with a slow and shuffling gait, developed 18 months before admission to hospital. For 12 months he had been liable to outbursts of unwarranted laughter and weeping, and had deteriorated mentally.

He was fatuous and expressionless, but euphoric. He had little insight and cerebration was slow. There was a defect of conjugate upward gaze with sustained nystagmus to the right and also when looking upwards, and a coarse nystagmus to the left. The face was spastic and the jaw-jerk increased; clonus could be obtained at times. There was also increased tone in the flexors of the neck, with rigidity of all muscle-groups in the right arm and in both legs, with moderate adductor hypertonus and bilateral spastic foot-drop with



(a) (b)

Fig. 5—Case 2. (a) Lymphocytes and microglia surrounding venule in regions of nuclei pontis (paraffin, hæmatoxylin and eosin ; ×290). (b) Cuffing of capillary and venule with "foam-cells" in ventral corticospinal tract at level of C7 (paraffin, hæmatoxylin, and eosin ; ×70).

contractures. The plasma-fibrinogen level was sometimes raised to 800 mg. per 100 ml. Lumbar puncture provided a clear and colourless fluid with 6 cells (50% polymorphs) per c.mm., protein 90 mg. per 100 ml., Lange 11111100000.

The illness was steadily progressive. Tetraplegia and dysphagia ensued, speech became difficult and unintelligible, and he died of bronchopneumonia some 2 years after the apparent extension of disease into the central nervous system.

Necropsy

A virological examination was made immediately after death (Evans et al. 1957). Only a limited necropsy was permitted. We are grateful to Dr. J. B. Raffan for permission to study the brain.

The brain (fixed) weighed 1380 g. The leptomeninges were a little thickened over the anterior part of the vertex, with milkiness in the depths of the sulci, against which the veins, which were generally distended, showed up well. The blood-vessels appeared normal. The brain stem was detached at the level of the upper part of the pons to expose a deformed right crus. The ventricles were not dilated.

Histology

Cerebral cortex.—Representative parts of the frontal, temporal, occipital and pre- and post-central cortex and insula showed no softenings or other abnormality. There appeared to be no loss of cells. The cornu Ammonis was normal apart from a little lymphocytic cuffing of vessels in relation to the stratum granulosum of the gyrus dentatus, and in places an increase of glial fibres in the external molecular layer. The central white matter was mostly healthy, but there was some patchy loss of myelin in the corpus callosum.

Basal ganglia.—Dilatation of capillaries, increased activity of the microglia, and in one place cuffiing of a grossly dilated venule in the claustrum. The nerve-cells here as elsewhere appeared to have a high lipid content, but were otherwise normal.

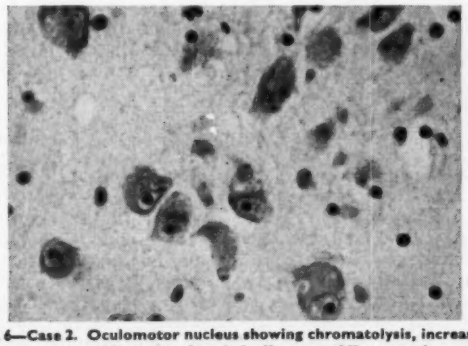


Fig. 6—Case 2. Oculomotor nucleus showing chromatolysis, increase of lipochrome, and intracytoplasmic bodies resembling granulovacuolar degeneration (celloidin, cresyl violet ; ×280).

In the caudate nucleus, putamen, globus pallidus, and thalamus, there were no softenings and no loss of cells. In the fornix, external medullary lamina, and internal capsule, including especially the sublenticular part, there were many small softenings, in the vicinity of the largest of which were hæmosiderin-filled macrophages ; occasionally there was slight cuffing with lymphocytes ; the lower part of the internal capsule and the crura in fact showed more damage than anywhere else. The cells of the corpora Luysii showed much intracytoplasmic lipid and there was cuffing of vessels in the corpora mammillaria : small softenings were seen around the third ventricle. The optic nerves and chiasm, third nerve, and anterior and posterior spinal nerve-roots appeared normal, but there was patchy loss of myelin around slightly cuffed blood-vessels in both optic tracts.

Mid-brain.—Small foci of softening, few in number, mostly central, the largest being in the decussation of the brachia conjunctiva. Lymphocytic cuffing of vessels was here a noticeable feature. The cells of the oculomotor nucleus were mostly swollen, and the Nissl substance was confined to the periphery : sometimes the nucleus had an irregular outline or was completely obscured. The nucleoli were occasionally unduly prominent, but intranuclear inclusion-bodies were not seen. The cytoplasm often contained many coarse granules, orange-red in colour, which appeared to be a lipofuscin : occasionally, however, the granules were fewer, even solitary but larger ; they lay in vacuoles and appeared to be surrounded by a pale halo. A few of them, but not all, were P.A.S.-positive. Two examples of twin cells were noted, and a few corpora amylacea. There was no gliosis. The pigmented cells of the substantia nigra appeared healthy and in normal numbers, and there were no inclusion bodies. *Pons*: Softenings rather more frequent and cuffing of vessels more prominent ; much microglial activity around the softenings, especially the smaller ones. Changes in the cells of the nuclei pontis resembled those in the oculomotor nuclei (figs. 5*a* and 6). In the lower pons some vessels showed swellings of the media with some loss of cellularity. *Medulla*: Focal softenings with perivascular infiltration were as numerous as in the pons. Both pyramids were degenerated. The cells of the olives appeared normal but for an occasional instance of neuronophagia.

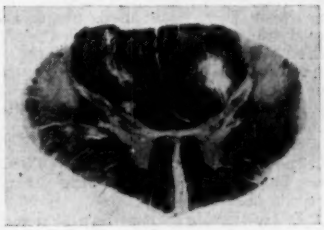


Fig. 7—Case 2. Spinal cord at level of D2, showing bilateral degeneration of lateral and ventral corticospinal tracts and fasciculus interfascicularis, and multiple focal softenings (celloidin, Heidenhain; ×4).

Cerebellum.—No significant lesions were seen in the cortex, but there were very occasional glial nodules in the white matter. In the dentate nucleus, there were a few instances of neuronophagia, and sometimes small aggregates of microglial cells not in relation to nerve-cells ; there was a slight general increase in glia.

Spinal cord.—In the cervical cord there was degeneration of both lateral and anterior corticospinal tracts and of the fasciculus interfascicularis (figs. 5*b* and 7) ; there were also localised and irregularly shaped but not very sharply defined areas of demyelination in the anterior, lateral, and posterior columns of varying size, some of which at any rate appeared to be focal softenings with fat-filled macrophages clustered around blood-vessels. The anterior-horn cells appeared healthy. The pyramidal-tract degeneration was visible throughout the cord.

Neurological Lesions

Previous Cases

The neuropathological findings previously described may be summarised as follows :

Berlin (1944) reported the case of a man aged 28, whose terminal symptoms of headaches, dizziness, apathy, confusion, disorientation, and fits lasted 3 months, starting when he had had the disease for $5^1/_2$ years and eye symptoms for 2 years. The basal meninges were thickened. Round cells and a few neutrophils were found in the meninges and brain-stem lesions; pseudoxanthoma cells were seen in the small scattered old necrotic foci in the substantia nigra and floor of the third ventricle. The spinal cord was œdematous but the peripheral nerves normal. The choroid and membranes of the optic nerve were infiltrated with cells and the central artery of the retina was cuffed.

Silfverskiöld (1951) found multiple foci of cellular infiltrations (mainly in the peduncles, brain stem, thoracic cord, and right optic tract), with perivascular round-cell infiltration. He speaks of "large areas of ramollation formation" and of a perivasculitis deep to the fourth ventricle. In the areas of cellular infiltration, axis cylinders were partially missing and fat-granule cells were present. The pons, pyramids, and cervical cord were swollen, and the pallidum was described as having an unusual blue-grey colour. The patient was a man, aged 19, who lived 19 months after the onset of papillitis and bilateral choroidoretinitis, preceded by several years of blepharoconjunctivitis. Recurrent spastic paraplegia developed a year after the onset, and during his last 5 days there were symptoms of bilateral facial weakness, a right sixth nerve palsy, and quadriplegia. Wadia and Williams (1957), it should be noted, reject this case, as only one of Behçet's triad of symptoms (mouth, genitalia, and eyes) was present.

Magni's (1951) patient was a soldier who, after 5 years of illness without genital lesions, began to have transient attacks of paræsthesiæ, pareses of the third nerves and of the legs, tremors of the left arm and tongue, right facial weakness, impaired elevation of the right eye, and bilateral pyramidal signs. Later there was bradykinesia, tremor of the jaw and upper limbs, a facies suggestive of parkinsonism, dysarthria, slight bilateral ptosis, nystagmus, and mental impairment. At necropsy there was much meningeal thickening, especially over the chiasm, with slight external hydrocephalus and an irregularity of the substantia nigra.

Alema and Magni (1952) found degenerative changes in the neurones of the grey matter, and especially the thalamus, substantia nigra, oculomotor nuclei, and hypothalamus, characterised by glial proliferation and infiltrations composed of mononuclear and "rod" cells. There were hæmorrhages in the mesencephalon. Neutrophils were seen around some of the blood-vessels. There were no significant changes in the myelin sheaths.

To these findings may be added certain observations on the general pathology of Behçet's disease. Prosser Thomas (1947) noted venous thrombosis in lesions of the skin at biopsy, and France et al. (1951) found that the earliest lesions consisted of perivascular and interstitial œdema with infiltrations of small mononuclear cells and lymphocytes around the capillaries and veins, the arterioles being spared. Jebejian and Kalfayan (1946), on ophthalmoscopic examination, observed an inflammatory process surrounding the smallest veins, often accompanied by hæmorrhage and at times by a sudden thrombosis. Finally there is the report by Hogan (cited by Sezer 1953) on an enucleated eye which showed marked inflammation of the disc and a necrosis of the nerve-fibres and glial bundles on the surface of the disc. The optic nerve-fibres were extensively atrophied. From this eye, Sezer isolated a virus which produced, in the brain of mouse and rabbit, the picture of an encephalomyelitis with glial proliferation and typical nodular foci.

Present Cases

In the first case the lesions were widespread and advanced: the upper brain stem, the basal ganglia, and the cerebral cortex were extensively involved and there were major ischæmic lesions in the left temporal and occipital lobes. The lesions seemed to be of four types:

(1) Foci of softening in relation to blood-vessels with moderate microglial activity, rather feeble astroglial proliferation, and, when involving grey matter, loss of nerve-cells.

(2) Perivascular cellular infiltrations with lymphocytes and occasional microglial cells, mostly in the white matter and with slight associated loss of myelin.

(3) Perivascular cuffing with sudanophilic foam-cells mostly in the white matter.

(4) Extensive and patchy areas of cortical infarction with consecutive astroglial proliferation.

The lesions in the second case were neither so plentiful nor so severe, and were largely confined to the upper brain stem. They were of three types, two of them corresponding to (1) and (2) above. The third consisted of small foci of microglial activity in both white and grey matter. The nerve-cells, more particularly those in the brain stem, were sometimes abnormal, containing an excess of lipochrome and occasionally intracytoplasmic granules of unidentified type, which at times resembled the granulo-vacuolar degeneration of Simchovicq. Alzheimer's neurofibrillary degeneration was not seen.

The nerve-cell changes were more pronounced in case 2, but in neither were intranuclear inclusion-bodies identified. In the cortical lesions in case 1, the contiguous nerve-cells, contrary to expectation, often appeared healthy. Axons occasionally transversed the smaller lesions but more usually appeared unduly thin and beaded; in the larger lesions they were not seen.

Apart from the focal lesions, changes in the cerebral cortex were only slight in case 1 and virtually absent in case 2. In the white matter of case 1, there was a diffuse loss of myelin and many focal softenings. In both cases the multiple lesions involved the spinal cord as well as the brain, but it was sometimes hard to distinguish focal softenings from tract degeneration.

The virtual immunity of the cerebellum in both brains is noteworthy: the integrity of the Purkinje cells does not suggest any important anoxic episodes during the epileptiform seizures in case 1 or during the terminal hyperpyrexia in case 2.

In both cases most of the lesions probably originated in relation to the smaller blood-vessels. Capillary or venous thrombosis, however, must be judged unproven, because apart from the presence of fibrin in the lumen of some of them (perhaps an agonal phenomenon) and a very occasional instance of vascular recanalisation (which could be a secondary event), no vessels were seen in an active stage of thrombosis, though many softenings were studied. But, since the disease is chronic, the possibility of thrombosis cannot be excluded. The presence of intracellular blood-pigment adjacent to many of the softenings might be due to thrombosis, or, equally, to repeated episodes of diapedesis resulting from altered vascular permeability.

The neurological symptoms and signs in case 1 are incompletely recorded, but there were enough lesions in the internal capsules (especially on the right) and in the brain stem to account for the spastic paraplegia and the paralysis of the right arm. The frequent fits can be ascribed to the large number of cortical softenings, which were fairly evenly spread throughout the hemispheres including the precentral cortex. In case 2, the involvement of the internal capsules explains the tetraparesis; the softenings in the medulla the dysarthria and dysphagia; and the lesions of the oculomotor and other brain stem nuclei the disordered eye movements.

The pathological findings in these two cases are in keeping with those reported by Berlin, Silfverskiöld, and Alema and Magni. Our case 1 seems the most severe of the five, while the brain stem is constantly involved in all of them.

The lesions in the brains should be related to the cerebrospinal-fluid findings. At lumbar puncture, our patients had normal or only very slightly raised cell-counts. The meningeal reaction might best be described as of a reparative character. A pleocytosis of 763 per c.mm. has been reported by Gray (1950), and 1260 (80% neutrophils) and 235 (31% neutrophils) by Silfverskiöld (1951, second and third cases). The counts in other patients have varied from 0 to 95, but, even when the figure has only been slightly elevated, it has been usual to find a few neutrophils. It is evident therefore that the meningeal component of the disease may be appreciable in some cases, especially during phases of activity.

A first-zone gold-curve was noted by Pallis and Fudge (1956) in the lumbar fluid of their case 1, associated with a protein

content of 510 mg. per 100 ml.; but even in the cisternal fluid, which had a protein content of 70, the reading was 4444322110, and this implies a relative increase in the γ-globulin fraction. First-zone curves are common in inclusion-body encephalitis, in the meningo-encephalitis of lymphogranuloma venereum (Zarafonetis 1944, Scott 1945) and in other infections and conditions in which antibodies are believed to be formed. In view of the alleged short-lived immunity in Behçet's disease, serial observations on the cerebrospinal-fluid globulins would be valuable.

Discussion

A noteworthy feature of Behçet's disease is its geographical preference for the Eastern Mediterranean basin, where Hippocrates seems to have been the first to describe as an endemic disorder what we know now as the triad of Behçet (Feigenbaum 1956). Our first case, a native of Western Australia, lived in Perth where cases have already been reported (O'Donnell 1947, Linton and Saint 1956); O'Donnell's patient was a Greek. Gottsegen and Korossy's (1956) patient contracted the disease while a prisoner-of-war in the Mediterranean, while Zeavin et al. (1956), in reporting the third example in an American-born citizen, note that he had worked in a shipyard, and that there he had first had the rheumatic symptoms which so often seem to initiate the disease. It is not uncommon in England, but is by no means confined to seaports, for Phillips and Scott (1955) found 10 cases in Birmingham gynæcological clinics. In Turkey, Sezer (1956) has reported it in three brothers. There seems little reason to doubt its infective character, and its tendency to relapse is notorious. Its relation to the Stevens-Johnson syndrome, Reiter's disease, Lipschutz's ulcer, Touraine's aphthosis, and various other mucocutaneous syndromes, is as yet uncertain.

The finding of a virus in case 2 by Evans, Pallis, and Spillane (1957) is in confirmation of the expectation of Behçet (1937), who found elementary bodies in the skin lesions, and of the virological claims of Alm and Öberg (1945) and Sezer (1953, 1956). Alm and Öberg produced focal encephalitis, optic neuritis, conjunctivitis, uveitis, and keratitis bullosa by intracisternal injection of cerebrospinal fluid into rabbits, and Sezer cultured a virus from the vitreous of an enucleated eye which caused encephalitis on inoculation into the brains of mice. He obtained serum complement-fixation and neutralisation reactions in known cases of the disease. In his more recent paper he finds that a temporary viræmia accompanies each attack of the disease, that the virus is excreted in the urine, and that complement-fixation reaches its maximum in 3 weeks and soon gradually falls. Immunity, therefore, is of short duration, and relapses are probably caused by auto-reinfection.

The degree of cuffing seen in our cases is not in itself sufficient evidence of viral infection; but, taken in conjunction with the chronicity of the disease, it may be considered compatible with it. Cuffing may, however, be inconspicuous or even absent in certain viral disorders of the brain, especially in the experimental encephalomyelitis of vesicular stomatitis (Sabin and Olitzky 1938).

A virus which involves the nervous system usually parasitises the more highly organised of the nerve-cells. There was little evidence of this, except for occasional instances of neuronophagia, which could be explained as the result of vascular disturbances and changes in the brain-stem nerve-cells in case 2. Nerve-cell changes, however, are not always a feature of viral infection of the nervous system; they may, for instance be very slight in the experimental encephalomyelitis of lymphogranuloma venereum (D'Aunoy and Von Haam 1939).

Our two cases leave the impression that the symptoms are related in the main to a series of minor, but anatomically important, vascular disturbances in the brain stem and elsewhere, which could have followed either a thrombosis or some other form of circulatory insufficiency.

The isolation of a virus from case 2 makes it necessary to ask how it could involve the central nervous system 15 years after the initial cutaneous symptoms. The relapsing character of the disease and the pathology might suggest that the mechanism of the brain disease is allergic in nature.

Kahle (1957) finds that the antigen-antibody reaction in all types of allergic encephalitis is strongest on the venous side of the circulation, where the mesenchyma is most likely to become sensitised against the waste-products of brain metabolism. The resulting inflammation may suffice to break down the pia-glial membrane. Our findings would fit in with this view, as in both cases the capillaries and veins, rather than the arterioles, were involved. Moreover, an allergic pathology seems likely, for in Behçet's disease swollen joints, erythema nodosum, erythema multiforme (our case 1), and occasionally eosinophilia are seen.

The disease bears little resemblance to post-infectious perivenous myelinoclasis, either in the distribution of lesions or in their essential character. The encephalomyelitis which follows revaccination, however, differs from that after primary vaccination, and our cases had some histological resemblance to the former, but differed in that the lesions were more widespread and were characterised by less myelinoclasis. After primary vaccination (Bastiaanse 1955), the demyelination spreads along the entire length of the implicated blood-vessels, there is extensive perivascular glial proliferation, and the nerve-cells are generally well preserved; but after revaccination the demyelinated areas are more localised (being almost exclusively at the junction of grey and white matter), are centred around capillaries, and have the shape of "an oil stain"; there is no striking perivascular proliferation of the microglia but there is pseudoneuronophagia and nerve-cell degeneration. Bastiaanse thinks that both forms are due to the virus or its component, but that the changes in revaccination possess an additional "allergic" character, the agent reaching the nerve-cells by way of the myelin sheaths. It must remain open to question whether the course of the disease in case 1 was modified or not by the treatment with "smallpox vaccine."

Judged by the histological findings, an allergic factor in ætiology is, we think, a possibility. But a virus was isolated in case 2 from a mixture of cerebrospinal fluid and white matter: if we accept it as the cause of the disease, we can just as readily hold it responsible for the lesions directly as by invoking an allergic mechanism. The individual neurological episodes could be explained therefore on the basis of recurrent viræmic phases, the paucity of inflammatory cells being attributed to the chronicity of the infection.

Case 1 bore some resemblance to inclusion-body encephalitis of Dawson type, and to reported cases of the closely related herpes-simplex encephalitis (especially to those of Haymaker [1949]) in that there was ischæmic necrosis of a temporal lobe with focal lesions of spongy necrosis in the lower laminæ of the cerebral cortex (see his case 1). But Haymaker's cases (which were virologically confirmed) were all of short duration, inflammatory phenomena were more evident, and no difficulty was found in identifying the intranuclear acidophilic inclusion bodies which are so distinctive of this disease. It should be remembered, however, that in several reported instances of this disease, inclusion bodies have not been found. It is of some interest to note that Haymaker failed to find in these acute cases any evidence of thrombosis of either the leptomeningeal or the cortical blood-vessels to account for the areas of ischæmic necrosis. Neither does Cambier (1955) make mention of thrombosis when he refers to the "véritable foyers" which suggested to him vascular softening.

It is tempting to assume that, because of its anatomical propinquity, the involvement of the eye carries with it a special liability to cerebral involvement and therefore is of more serious import to life than the oral and genital lesions. This might be expected from the experimental work of Sabin and Olitzky (1937), who found that the viruses of vesicular stomatitis and eastern equine encephalitis could be readily conveyed to the brain along the optic nerve. It might too appear to be supported by the fact that, of the eighteen reported cases of Behçet's

disease complicated by neurological involvement, the eyes were involved in fifteen. But ocular symptoms are as constant a feature of Behçet's disease as are the oral and genital lesions, and this high incidence of eye disorders cannot be deemed exceptional. Of greater significance are the facts that three cases (including our case 2) of Behçet's disease are known with neurological symptoms but no eye involvement, that in case 1 there was no histological evidence of spread along the optic pathway, and that the optic tracts were as much diseased in case 2, which had no eye symptoms, as in case 1.

It will now be seen that the resemblance to multiple sclerosis is little more than superficial. It is true that both diseases are relapsing in character, have pyramidal symptoms, ocular palsies, and multiple lesions with an anatomical predilection for the brain stem, and may be associated with a relative increase of globulin in the cerebrospinal fluid, as in case 2; but there the resemblance ceases, for in the encephalomyelopathy of Behçet's disease there is neither the extensive and varied pattern of demyelination nor the intense fibrous gliosis which characterises the former disease. In fact Behçet's disease is not a demyelinating disease in the usual meaning of the term. Moreover, the cord lesions tend to be peripheral in multiple sclerosis but more central in Behçet's disease; the cerebral lesions tend to be periventricular in multiple sclerosis, but not in Behçet's disease.

Summary

In two cases of Behçet's disease with clinical involvement of the central nervous system, the neuropathological findings are given and compared with three previous cases.

The lesions were multiple and had a distinctive pattern with a predilection for the hypothalamus and brain stem: they consisted in the main of innumerable small softenings in relation to the smaller blood-vessels and were seen rather more often in white matter than in grey. Inflammatory reaction was seldom obvious, and myelin loss appeared to be secondary.

The ways in which the central nervous system could become involved are discussed.

We are indebted to the Repatriation Commission of Western Australia for access to their records and for material for case 1, and to Dr. J. B. Raffan for his helpful coöperation in case 2. We also wish to thank Mr. Gordon Cox, F.I.M.L.T., and Miss Margaret Doe, A.I.M.L.T., for technical assistance.

REFERENCES

Alema, G., Magni, S. (1952) *Riv. oto-neuro-oftal.* **27**, 30.
Alm, L., Öberg, L. (1945) *Nord. med.* **25**, 603.
Bastiaanse, F. S. van B. (1955) *Folia psychiat. neerl.* **58**, 147.
Behçet, H. (1937) *Derm. Wschr.* **105**, 1152.
Berlin, C. (1944) *Arch. Derm. Syph., N.Y.* **49**, 227.
Cambier, J. (1955) *Presse méd.* **63** (ii), 286.
Critchley, M. (1957) Personal communication.
Curth, H. O. (1952) *Arch. Derm. Syph., N.Y.* **66**, 761.
D'Aunoy, R., Von Haam, E. (1939) *Arch. Path.* (*Lab. Med.*) **27**, 1032.
Evans, A. D., Pallis, C. A., Spillane, J. D. (1957) *Lancet*, ii, 349.
Feigenbaum, A. (1956) *Brit. J. Ophthal.* **40**, 355.
France, R., Buchanan, R. N., Wilson, M. W., Sheldon, M. B. jun. (1951) *Medicine, Baltimore*, **30**, 335.
Gottsegen, G., Korossy, S. (1956) *Derm. Wschr.* **133**, 33.
Gray, G. S. (1950) *Canad. med. Ass. J.* **62**, 597.
Haymaker, W. (1949) *J. Neuropath.* **8**, 132.
Jebejian, R., Kalfayan, B. (1946) *Ann. oculist., Paris*, **179**, 481.
Kahle, W., cited by Schaltenbrand (1957) Proceedings of the Second International Congress of Neuropathology. Amsterdam; p. 419.
Linton, R. G., Saint, E. G. (1956) *Med. J. Aust.* i, 502.
Magni, S. (1951) *Riv. oto-neuro-oftal.* **26**, 445.
O'Donnell, J. M. (1947) *Med. J. Aust.* i, 720.
Pallis, C. A., Fudge, B. J. (1956) *Arch. neurol. psychiat.* **75**, 1.
Phillips, D. L., Scott, J. S. (1955) *Lancet*, i, 366.
Sabin, A. B., Olitzky, P. K. (1937) *Amer. J. Path.* **13**, 615.
— — (1938) *J. exp. Med.* **67**, 201.
Scott, D. W. (1945) *Arch. intern. Med.* **76**, 174.
Sezer, F. N. (1953) *Amer. J. Ophthal.* **36**, 301.
— (1956) *Ibid*, **41**, 41.
Silfverskiöld, B. P. (1951) *Acta psychiat., Kbh.* **26**, 443.
Thomas, E. W. P. (1947) *Brit. med. J.* i, 14.
Wadia, N., Williams, E. (1957) *Brain*, **80**, 59.
Zarafonetis, C. J. D. (1944) *New Engl. J. Med.* **230**, 567.
Zeavin, B. H., King, M. J., Gohd, R. S. (1956) *Amer. J. Ophthal.* **41**, 55.

CELLULITIS AND THROMBOPHLEBITIS IN BEHÇET'S SYNDROME

G. R. CARR
M.D. Michigan, Ch.M. Manc., F.R.C.S.
SENIOR SURGICAL REGISTRAR, ROYAL INFIRMARY, MANCHESTER

IN 1937 Behçet recommended that the triad of recurrent oral and genital ulceration with relapsing iritis be considered a disease entity, and since then this syndrome has borne his name.

Although most patients with this condition usually attend an ophthalmological or a dermatological clinic, the initial symptom for which advice is sought may be one of general medical or surgical interest. The case reported here was referred to the department of surgery of the Royal Infirmary, Manchester, with a diagnosis of thrombophlebitis, a common lesion in outpatient clinics.

Most of the published cases have been in young adult males inhabiting the eastern shores of the Mediterranean but several cases have now been reported in this country, including ten cases in $3^1/_2$ years by Phillips and Scott (1955).

The main lesions may be described briefly:

Eyes.—The characteristic eye lesion is iridocyclitis with hypopyon. Both eyes are affected, sometimes simultaneously and sometimes separately. The ocular crises are recurrent, developing at intervals of 1–2 months over a period of years. Vision usually becomes progressively less.

Genitalia and mucosæ.—Ulcers of the mouth and scrotum are usually multiple and may begin as superficial erosions or as indurated nodules. The base may be either clean or filled with yellow slough. In females the genital ulcers are mainly confined to the vulva but may develop in the vagina or in the cervix, causing a purulent discharge. The oral ulcers may cause pain on mastication and heal in about 2 weeks, but usually recur.

Subsidiary lesions.—Apart from the primary triad of symptoms, in nearly all the cases there are associated complaints, which may be of greater immediate concern to the patient. These include skin lesions resembling erythema nodosum, erythema multiforme, monarticular arthritis (sometimes with effusion of sterile fluid), various lesions of the central nervous system, and thrombophlebitis. Cellulitis, which was the presenting sign in the present case, does not appear to be common in Behçet's syndrome.

Case-report

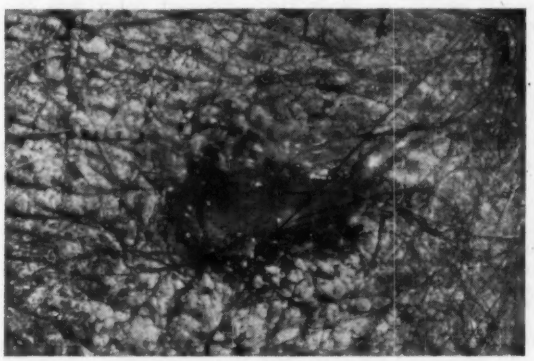
A plumber's apprentice, aged 17, was referred to the Manchester Royal Infirmary from another hospital in April, 1955, with 2 years' history of recurrent swelling with tenderness, redness, and increased local temperature of his left thigh, calf, and ankle. The first attack started after he had strained his left leg when working on a roof. This subsided in a few days after rest and a course of penicillin. The condition recurred in January, June, and September, 1954, and each time the swelling subsided after a course of penicillin.

In February, 1955, 10 days after a minor injury to the left thigh, he developed swelling, tenderness, and redness in the thigh. Investigations revealed a white-cell count of 18,000 per c.mm., and an erythrocyte-sedimentation rate (E.S.R.) of 30 mm. (Wintrobe) in 1 hour. Radiographs of his femur and chest were normal. Agglutination tests for brucellosis and the typhoid group were negative.

The patient's condition settled down in a few days with rest alone. But, as he was thought to have an unusual form of thrombophlebitis migrans, he was referred to the vascular clinic at the Manchester Royal Infirmary, where he was admitted for investigation in May, 1955.

First Admission

He then had an area of cellulitis measuring 15 × 10 cm. on the medial aspect of the upper part of his left thigh. This cellulitis had appeared 3 or 4 days before admission and progressed rapidly. His temperature was 104°F, and he appeared very ill. For the first time a history was elicited of three years' recurrent ulceration of his mouth and scrotum, and several ulcers were found on his scrotum (see figure). These were superficial, about 1–2 cm. in diameter, with a yellow base, a shelving edge, and no surrounding induration.



Scrotal ulcer.

There was a similar ulcer on the side of the tip of his tongue, together with scars of previous lesions.

Penicillin was given and on the 3rd day his temperature was normal, although the cellulitis was still present. On the 9th day superficial thrombophlebitis developed in his right antecubital fossa and extended up the basilic and cephalic veins to the upper third of his arm during the next few days and was associated with a pyrexia of 101°F. There was no history of venepuncture at this site. On the 18th day the lesions were subsiding but he still appeared ill.

Investigations

During the illness his blood-count was normal. E.S.R. 48–51 mm. in 1 hour. Serum-albumin 3·6 g. per 100 ml.; globulin 3·7 g.; sodium 138 m.eq. per litre; potassium 5·4 m.eq.; chloride 98 m.eq. Mantoux test 1 : 10,000 strongly positive, producing an area of erythema and induration 8 cm. in diameter, with a necrotic centre exuding pus, and a temperature of 103°F.

On the 30th day he was started on a 10-day course of aureomycin (chlortetracycline) 250 mg. 6-hourly, with improvement in his general condition and healing of all lesions. He was discharged on June 13, 5 weeks after admission.

Readmission

A month later he was readmitted with 3 days' history of a throbbing pain in the medial aspect of his right thigh. It had come on a few hours after someone had trodden on his right foot, when he felt pain in the thigh on withdrawing his foot.

He was found to have a tender thickening along the course of the long saphenous vein, but no redness. He also had herpetic lesions at the angle of his mouth and two small painless shallow ulcers on his fauces.

Treatment with corticotrophin 30 mg. b.d. was begun. A week later œdema of his right ankle and tenderness of his right calf developed but subsided over the next few days, and he then developed a pain behind the right knee on extension. In the popliteal fossa was a tender hard cord. The knee was held in flexion. This pain subsided in a few days. The general condition remained excellent while under treatment with corticotrophin, and he was discharged on a maintenance dose of 10 units b.d.

Follow-up

During the succeeding 12 months he remained well, apart from recurrent oral ulceration, but these attacks were of greatly reduced frequency.

Discussion

Curth (1946) and Phillips and Scott (1955) suggested that the diagnosis should be applied when two of the three main features are present, and in this regard it should be noted that the oral and genital ulceration may precede the ocular symptoms by many years.

The diagnosis of Behçet's syndrome in this case was based on the presence of two of the primary triad of symptoms, together with the subsidiary symptom of thrombophlebitis, which has been reported in more than a quarter of 33 cases by France et al. (1951). The attacks, both of cellulitis and thrombophlebitis, on several occasions followed minor trauma—possibly this fact is a reflection of increased tissue sensitivity to trauma.

A similar phenomenon of "non-specific skin sensitivity" and "skin-puncture sensitivity" was reported by France et al. (1951). The latter is described as a tendency on the part of the dermis to react to the prick of a sterile needle with a painful red nodule or a pustule. The extreme reaction to 1 : 10,000 Mantoux reagent in the reported case was probably another manifestation of this phenomenon.

Ætiology.—Two possible causes have been suggested. Behçet originally thought that a virus was responsible, but other workers have believed a collagen disorder to be the underlying factor. Sezer (1953), however, has produced strong evidence that Behçet's syndrome is caused by a virus; he has isolated a virus from 3 patients. The virus was obtained from exudate collected from under the retina and from the vitreous body of enucleated eyes. This virus produced in rabbits a disease very similar to that in man. Sezer's studies therefore appear to confirm that this syndrome is indeed an entity.

Treatment.—No particular treatment has been shown to be successful and, as in most diseases with spontaneous remissions, assessment of treatment is difficult. Aureomycin was given to the present patient in view of the possible virus ætiology; but although the lesions healed they recurred later. Corticotrophin, given after his second admission to hospital, improved his general condition considerably and kept him free from all symptoms other than oral ulceration, which recurred less frequently than before. In the present patient, therefore, corticotrophin appears to have produced definite clinical improvement.

Summary

A case of Behçet's syndrome is reported.

The development of cellulitis in this patient is an unusual occurrence in Behçet's syndrome and may be another manifestation of non-specific tissue sensitivity previously reported.

Either thrombophlebitis or cellulitis may be the initial symptom for which advice is sought.

I should like to thank Prof. A. M. Boyd for permission to publish this case.

REFERENCES

Behçet, H. (1937) *Derm. Wschr.* **105**, 1152.
Curth, H. O. (1946) *Arch. Derm. Syph., N.Y.* **54**, 179.
France, R., Buchanan, R. N., Wilson, M. W., Sheldon, M. B. jun. (1951) *Medicine, Baltimore*, **30**, 335.
Phillips, D. L., Scott, J. S. (1955) *Lancet*, **1**, 366.
Sezer, F. N. (1953) *Amer. J. Ophthal.* **36**, 301.

THE TOXICITY AND FATE OF INJECTED ANIMAL ANTIHÆMOPHILIC GLOBULIN

A. A. SHARP
M.B., B.Sc. Edin.
GRADUATE ASSISTANT

E. BIDWELL
B.Sc., Ph.D. Lond.
GRADUATE ASSISTANT

UNIVERSITY OF OXFORD

From the Radcliffe Infirmary, Oxford

THE successful use of concentrated antihæmophilic globulin (A.H.G.), prepared from bovine and pig blood, in promoting effective hæmostasis in hæmophilia, has been described by Macfarlane, Biggs, and Bidwell (1954), Fraenkel and Honey (1955), and Macfarlane et al. (1957). The present paper describes the animal experiments carried out to determine any ill effects produced by long-continued or massive dosage. The preparations used were made by the method of Bidwell (1955a and b) and contained large amounts of fibrinogen, and probably small amounts of other plasma proteins, as well as the antihæmophilic factor. Two kinds of toxic effect might be expected, one due to increased coagulability of the blood and the other to the injection of a mixture of heterologous proteins. The experiments were designed to differentiate between these as far as possible.

It was also desirable to know how these heterologous proteins are distributed in the body and how long they persist. The production of precipitating antibodies by the injection of these materials into rabbits led to the possibility that the conjugated fluorescein-antibody technique of Coons et al. (1942) and Coons and Kaplan (1950) might be useful in tracing the fate of these heterologous proteins in humans and animals.

Methods

Antihæmophilic globulin (*A.H.G.*) (bovine, pig) was prepared by the method of Bidwell (1955a and b). It was dialysed and sterilised by Seitz filtration (Bidwell 1955b).

Assays of antihæmophilic activity were done under the supervision of Dr. Rosemary Biggs using the method of Biggs, Eveling, and Richards (1955).

Dosage of A.H.G.—In this paper "one human dose" of heterologous A.H.G. is that amount which would provide antihæmophilic activity approximately equal to that contained in 2500 ml. of fresh human plasma as assayed by the method of Biggs et al. (1955). This is equivalent to about 600 units of activity as defined by these workers. The corresponding amount of heterologous protein varies with the degree of purity of the preparation used, there being about 200–400 mg. protein in one human dose of the material given to hæmophilic patients; up to three times this amount has been given in an actual clinical dose. Material of maximum purity could not be spared for these experiments and thus one human dose of the material used in the animal work, corresponding to 70 kg. body-weight, might contain 1 g. or more of foreign protein. Animal doses of A.H.G. were scaled down in proportion to body-weight—e.g., for a rabbit weighing 3·5 kg. the equivalent of one human dose would be 30 units of A.H.G.

Preparation of Specific Antibody to Pig and Bovine A.H.G.

Antisera were prepared in rabbits against both bovine and pig A.H.G. concentrates at the Wellcome Research Laboratories using standard techniques (Proom 1943); it was found that they cross-reacted with both antigens and with human fibrinogen to a high titre using precipitin-ring tests; although the agar-gel diffusion technique of Ouchterlony (1949) also showed a reaction between the heterologous antigen and antisera it was of different and readily distinguishable type from that given by the homologous antigen.

The cross-reaction with human fibrinogen was abolished by absorption and the antibodies were concentrated by fractional precipitation of the globulin fraction by half saturation with ammonium sulphate. Conjugation of these rabbit-serum globulin fractions with fluorescein isocyanate was effected by the method of Coons and Kaplan (1950).

In the present experiments the antisera when combined with fluorescein amine, appeared to be quite specific for the homologous antigen, no cross-reaction being demonstrable.

Preparation of Tissue for Fluorescent Microscopy

The tissues to be examined were rapidly frozen by placing in a glass container surrounded by an acetone-solid CO_2 mixture. Histological sections were prepared by the use of a cryostat identical with that described by Coons et al. (1951). The sections were thawed on to glass slides, dried in air, and stored at 4°C. As the material to be demonstrated was a heterologous globulin, all the sections were fixed in 95% absolute alcohol for 30 minutes (Coons et al. 1951). Residual unconjugated fluorescein was removed by absorption with acetone-dried guineapig liver or muscle powder before application to the fixed and dried sections. The sections were stained with the appropriate conjugated and absorbed antisera for 2 hours at room-temperature or 18 hours at 4°C. Following the staining process the slides were washed in saline (buffered to pH 7·0) for 10 minutes and then mounted in buffered glycerol (1 part buffered saline to 9 parts glycerol). A cover slip was applied and the preparations examined microscopically using an ultraviolet-light source. The presence of the characteristic apple-green fluorescence of the conjugated fluorescein in any part of the tissue indicated that the conjugated antibody had become selectively attached to this particular tissue, which could therefore be presumed to contain the specific antigens which in this particular study were present in the preparations of bovine or pig A.H.G.

It was essential to confirm the significance of a positive result by treating a duplicate section with non-conjugated specific antibody (anti-pig or anti-bovine A.H.G.) before addition of the conjugated antibody (Coons and Kaplan 1950). This should inhibit completely the subsequent union with the conjugated antibody.

Results

TOXICITY OF HETEROLOGOUS A.H.G.

General Toxicity

About eighty batches of bovine and pig A.H.G. have been tested for general toxicity by subcutaneous injection of 2–5 mg. protein in 0·2 ml. solution into each of five mice, which were allowed to survive for at least a month. None of the animals showed any systemic disturbance following these injections. Occasional deaths occurred but in no instance could any damage attributable to the injection of these materials be demonstrated histologically.

Lethal Dose of A.H.G. in Animals

Three dose schedules were adopted using both preparations:

(1) 10 equivalent human doses were given intravenously in 1 minute to four rabbits, two receiving pig A.H.G. and two bovine A.H.G. The total volumes injected were 10 and 16 ml. respectively for bovine and pig A.H.G.

(2) 50 equivalent human doses were given in 17 separate injections over a period of 6 hours to two rabbits, one receiving pig A.H.G. the other bovine. The total volumes injected were 84 and 88 ml. respectively for bovine and pig A.H.G.

(3) 50 equivalent human doses were given in one injection within 1 minute to two rabbits, one receiving pig A.H.G. and the other bovine. The total volumes injected were 35 and 50 ml. respectively for bovine and pig A.H.G.

In these experiments the number of animals was restricted by the amounts of these concentrates available for testing.

All surviving animals were killed 24 hours after administration of the A.H.G. and their tissues examined histologically.

In groups 1 and 2 above no obvious clinical abnormality was noted during the injections or in the 24 hours after injection. In group 3 the animal receiving pig A.H.G. collapsed and died after 25 ml. (equivalent to 25 human doses) had been injected. The rabbit receiving bovine A.H.G. collapsed after the equivalent of 50 human doses had been given but recovered and survived until killed 24 hours after the injection. In both instances the episode of collapse was associated with apparent acute air-hunger, cyanosis, peripheral circulatory collapse, and unconsciousness. In the one animal which survived, the episode of collapse persisted for approximately 5 minutes, to be followed, on recovery of consciousness, by dyspnœa and tachypnœa persisting for at least 4 hours. Intravenous injections of an equivalent volume of sodium citrate *or* 1% bovine albumin (Armour) within 30 seconds did not produce any clinical disturbance.

Post-mortem Examination

In all these experiments, only one animal showed any significant macroscopic lesions.

These were observed in the rabbit which died immediately after the injection of 25 human doses of pig A.H.G. Its lungs were generally congested and appeared to be partially collapsed. Histological examination confirmed these conclusions. The alveolar capillaries and pulmonary veins showed extreme congestion with associated focal intra-alveolar œdema and collapse.

In the tissues obtained from the other animals injected with heterologous A.H.G. no significant histological changes were apparent.

Effect of Repeated Daily Injections of Heterologous A.H.G.

Repeated injections of either bovine or pig A.H.G. into hæmophilic patients eventually produced allergic reactions, and in addition bovine A.H.G. was shown to cause striking but transient thrombocytopenia. Pig A.H.G. was not found to affect platelets in vivo (Macfarlane et al. 1957).

To simulate the normal pattern of therapy adopted to treat cases of hæmophilia, rabbits were given daily intravenous

injections of 2 human doses of either pig or bovine A.H.G.; two rabbits initially received bovine A.H.G. and two pig A.H.G. No clinical abnormality was observed until the 9th day, when both rabbits receiving pig A.H.G. were profoundly disturbed by the injection and had an anaphylactoid type reaction with acute dyspnœa persisting for 30 minutes. No such reaction took place with bovine A.H.G.

As it was not intended to measure the tissue changes of anaphylaxis, on the following day the alternative preparation was given and daily injections were continued until the 16th day when all animals were killed and their tissues examined. No further clinical upset was apparent during this last 7 days.

During this series of experiments, platelet-counts were performed before and 5 and 30 minutes after injection of the A.H.G. preparations. No abnormality was noted until the 8th day when both preparations produced a profound thrombocytopenia within 5 minutes of the injection being given. The platelet-count had begun to rise again after 30 minutes and had returned to normal within 24 hours. The anaphylactoid reaction on the 9th day was also associated with a definite fall in the platelet-count. After the change over to the alternative preparation, this thrombocytopenic effect of the A.H.G., although at first less marked, persisted and was fully re-established on the 13th day. It was still transient, and in one instance the platelet-count had returned to normal levels 30 minutes after the injection.

In-vitro Platelet Agglutination by A.H.G.

Agglutination of either washed human platelet suspensions or platelets in plasma could be produced in vitro by small amounts of bovine A.H.G. (0·5 mg. per ml.). This reaction took place within 2 minutes of adding the A.H.G. preparation. When used in similar concentrations, pig A.H.G. had no effect; but when it was used in ten times the concentration (5 mg. per ml.) similar platelet agglutination could be demonstrated. This reaction was apparently peculiar to human platelets, for no reaction could be produced with either bovine or pig A.H.G. when added to platelet suspensions from rabbits, mice, rats, guineapigs, cats, dogs, cow, or pig, in concentrations of 10 mg. per ml.

FATE OF INJECTED A.H.G.

When heterologous animal A.H.G. is injected intravenously into patients with hæmophilia, its presence can be detected in the blood by its coagulant activity. Quantitatively the activity never approaches that expected from simple dilution in the patient's plasma, and decreases rapidly, virtually disappearing within 24 hours.

Distribution of A.H.G. in Human and Animal Tissues

Post-mortem tissues were obtained from three cases of classical hæmophilia treated by A.H.G. at varying times before death.

(*a*) Pig A.H.G. last administered 24 hours before death (case 10, Macfarlane et al. 1957).

(*b*) Bovine A.H.G. last administered 3 days before death (case 11, Macfarlane et al. 1957).

(*c*) Bovine A.H.G. last administered 7 hours before death. This patient, described by Macfarlane et al. (1957) (case 16) was admitted to the Central Middlesex Hospital some months later with a suspected subdural hæmorrhage. To allow surgical intervention, bovine A.H.G. was supplied and administered. At operation the patient was found to have a cerebral hæmorrhage from which he died, without regaining consciousness, 7 hours after the last injection of bovine A.H.G.

Four normal rabbits and six mice were injected intravenously with A.H.G. in amounts equivalent to two human doses. These animals were subsequently killed after varying times. In both human and animal tissue the fluorescent-antibody technique enabled injected foreign protein to be traced in the blood-vessels and capillaries. The specific fluorescence observed suggested that well-defined clumps of foreign protein existed in vivo, either adhering to the vascular endothelium, lying free in the blood-stream, or in many instances apparently blocking small tissue capillaries in the lung, muscle, heart, liver, and kidney. In the latter organ specific fluorescence was especially prominent in the capillaries of the glomeruli.

In animals this material had disappeared entirely within 24 hours. Trace amounts were found in the human cases 7 and 24 hours after injection but none after 3 days. In no instance could heterologous protein be detected in any other normal tissue. It did not become localised in the cells of the reticulo-endothelial system as does heterologous γ globulin (Coons et al. 1951), nor was there any detectable A.H.G. activity in the urine of patients and animals after intravenous injection of A.H.G.

Incorporation of A.H.G. into Fibrin

Heterologous A.H.G. in human and animal wounds.—In only one instance was tissue available from a wound made in humans immediately after or during administration of animal A.H.G.

In case 10 (Macfarlane et al. 1957) the leg wound was made after the injection of bovine A.H.G. 14 days before death; bovine A.H.G. was administered up to 5 days before death, and pig A.H.G. for the 4 days before death. The wound fibrin showed the presence of bovine protein with no trace of pig protein, but (as reported above) only pig protein was detectable in the blood-vessels.

This finding suggested that injected bovine protein had been incorporated into or adsorbed on the fibrin as it formed and preserved its specific reactivity for at least one week.

To confirm this impression wounds, 2 cm. in diameter, were made in the flanks of two anæsthetised rabbits, after the injection of bovine or pig A.H.G. in amounts equivalent to two human doses. The wounds were allowed to heal undisturbed for 14 days, the animal was killed, and the wound was removed for examination. During the first period of this healing period the animals received daily injections of the original A.H.G. preparations and on the 7th day and subsequent days were given the alternative preparation. In both examples the wound fibrin showed specific fluorescence appropriate to the type of A.H.G. administered at the time of inflicting the wound. The specific conjugated antisera did not stain normal human or rabbit fibrin.

The experimental findings confirmed that one or other of the fractions of these heterologous proteins were incorporated or adsorbed on fibrin as it formed in the wounds. In no instance could any specific fluorescence be found in the granulation tissue or fibrous tissue adjoining the fibrin.

Homologous A.H.G. in animal wounds.—As it was important to attempt to identify the material demonstrable by specific staining in wound fibrin, biopsies from a pig and bullock were obtained. These were removed 1 hour, 48 hours, and 7 days after incisions 1 cm. in length had been made in the course of other experimental work at the Agricultural Research Establishment, Cambridge. The preparations were subsequently stained with the conjugated antisera.

In none of the preparations from these animals could any specific fluorescence be determined, although fibrin could be demonstrated by orthodox methods. Considerable non-specific fluorescence could be detected in that part of the exudate in the wounds rich in polymorph leucocytes. This interference was so marked in the 1-hour specimens that it could have obscured specific staining.

Addition of heterologous A.H.G. to blood of hæmophilic patients in vitro.—The following experiment was performed:

Citrated plasma obtained from a severely affected hæmophilic patient was clotted by the addition of an equal volume of M/40 calcium chloride both before and after the addition of 1/10 vol. of bovine and pig A.H.G. in a strength calculated to give a final concentration comparable to that used in clinical work.

The fibrin clots were removed and washed in saline, before freezing, sectioning, and staining as for ordinary tissues.

Heterologous protein could be stained by its appropriate conjugated antiserum in the fibrin of those plasmas to which A.H.G. had been added before clotting. No staining was evident in the fibrin obtained from unaltered hæmophilic

plasma, nor could it be shown in fibrin obtained from plasma to which pig fibrinogen had been added. The latter preparation had been made by the same process as the pig A.H.G. globulin but was found to have no A.H.G. activity on assay.

These results confirmed the specificity of the conjugated antibodies for the particular A.H.G. which had been used in their preparation.

Discussion

The toxicity of bovine and pig A.H.G. was evaluated on rabbits because these were the most convenient animals in which to inject relatively large volumes of fluid. Ideally these experiments should have been made on a species in which the platelets were agglutinated by these proteins in vitro; but, so far as our experiments have gone, only human platelets are affected in this way.

The antigenic properties of these proteins were clearly demonstrable in animals. Once immunity was established, transient thrombocytopenia was apparently provoked by each injection. The rapid reappearance of thrombocytopenia after changing to the alternative antigen was not accompanied by any obvious systemic reaction. These thrombocytopenic episodes, observed in the rabbit in association with the development of immunity to either bovine or pig A.H.G., are commonly a feature of anaphylactoid reactions. The thrombocytopenia seen in patients treated with bovine A.H.G. seems to have a different mechanism, since it follows immediately upon the first injection and is not produced by pig A.H.G.

With one exception, no significant tissue changes could be observed after single or repeated injections of large amounts of these foreign proteins. In the one animal which collapsed and died after the rapid injection of a concentrated solution of pig A.H.G. the main effect appeared to be on the lungs themselves, where the injected protein directly affected the pulmonary circulation either by reason of its viscosity or by promoting non-specific red-cell clumping. That this effect was peculiar to the A.H.G. concentrates was demonstrated by the similar but non-fatal reaction produced by a larger volume of bovine A.H.G., and the failure of equal volumes of citrate saline and bovine albumin to produce similar results. The volumes injected into these rabbits to produce these toxic changes would be approximately equivalent to administering intravenously 500–900 ml. of concentrated protein within 1 minute into a human being weighing 70 kg. Such volumes or concentrations have never been required in the treatment of hæmophilia, but these results do suggest that in cases of hæmophilia, with apparent resistance to A.H.G. therapy, abnormally large amounts of animal A.H.G. should not be given unless desperate measures are indicated.

The fate of heterologous A.H.G. has never been previously determined. That it behaves as a foreign protein and is antigenic there is no doubt; it differs from other foreign proteins in that it is not to be found in the reticulo-endothelial cells of the body, even after repeated injections. Thus very soon after injection it must either be destroyed or lose its ability to combine with specific antibody. In animals this had definitely occurred in 24 hours; a similar pattern was apparent in humans.

The appearance of the specific fluorescence in blood-vessels suggested that the injected A.H.G. might circulate as a flocculent precipitate and that this might be capable of inducing embolic phenomena. This finding is inconclusive because fixation of the sections before staining might produce this appearance by precipitation of the globulin in the blood-vessels. Staining of unfixed sections was unsatisfactory, as had previously been found for γ-globulin by Coons et al. (1951).

The discovery of persisting foreign protein in wound fibrin was significant. The conjugated antisera were apparently specific for their appropriate antigens and did not show any cross-reaction. The experimental results suggested that the conjugated antisera did combine with some protein other than fibrin derived from these heterologous proteins. Whatever the explanation, the observed concentration and persistence of heterologous animal A.H.G. or fibrin in the wound in a different species may explain the beneficial effects of this material on the integrity of the fibrin clot and the rate of healing in human hæmophilia (Fraenkel and Honey 1955). Its persistence in this site, while being destroyed rapidly in the circulation, is difficult to explain. The process of organisation immediately destroys the positive staining reactions; no specific fluorescence could be demonstrated in granulation or fibrous tissue.

Morphologically, the maximum fluorescence was visible at the periphery of the fibrin strands, and the wider and coarser the fibrin strand the more striking was the fluorescence. A similar appearance has been observed in the staining of fibrin by specific anti-fibrin conjugates in Gitlin and Craig's (1957) experiments. It was impossible to decide whether the foreign protein was incorporated in the fibrin or simply adherent to the periphery of the strands. Further experiments on these lines on more purified preparations of A.H.G. as they become available might reveal the degree of success in removing undesirable antigens.

Summary

The fate of heterologous animal proteins containing antihæmophilic globulin was determined by use of specific fluorescein-conjugated antisera. Evidence has been obtained to suggest that these proteins are concentrated in the wound fibrin of the recipient.

Their toxicity appears to be negligible except when given in very large doses. They are antigenic and may be expected to provoke varying allergic responses in a sensitised recipient.

We are indebted to Dr. Alan Hill and Dr. R. G. Scott of the Rheumatism Research Unit, Stoke Mandeville Hospital, for conjugating the antisera and for their constant advice and guidance; to Dr. C. L. Greenbury for laboratory facilities at Stoke Mandeville; to Dr. A. H. T. Robb-Smith for his advice on the histology; to Messrs. Maw for some of the animal antihæmophilic globulin; to the Wellcome Foundation for the preparation of antisera; to Sir Alan Drury and Mr. E. J. H. Ford of the Agricultural Research Establishment, Babraham Hall, Cambridge, and Mr. G. Fraenkel, for providing certain of the animal tissues; and to Dr. R. M. Stirland of the Central Middlesex Hospital for some of the human tissues. We are grateful to Mr. G. W. R. Dike for technical assistance.

REFERENCES

Bidwell, E. (1955a) *Brit. J. Hæmat.* **1**, 35.
— (1955b) *Ibid*, p. 386.
Biggs, R., Eveling, J., Richards, G. (1955) *Ibid*, p. 20.
Coons, A. H., Creech, H. J., Jones, R. N., Berliner, E. (1942) *J. Immunol.* **45**, 159.
— Kaplan, M. H. (1950) *J. exp. Med.* **91**, 1.
— Leduc, E. H., Kaplan, M. H. (1951) *Ibid*, **93**, 173.
Fraenkel, G. J., Honey, G. E. (1955) *Lancet*, ii, 1117.
Gitlin, D., Craig, J. M. (1957) *Amer. J. Path.* **33**, 267.
Macfarlane, R. G., Biggs, R., Bidwell, E. (1954) *Lancet*, i, 1316.
— Mallam, P. C., Witts, L. J., Bidwell, E., Biggs, R., Fraenkel, G. J., Honey, G. E., Taylor, K. B. (1957) *Ibid*, ii, 251.
Ouchterlony, O. (1949) *Acta path. microbiol. scand.* **26**, 507.
Proom, H. (1943) *J. Path. Bact.* **55**, 419.

"It often seems that the contemporary world is divided into two parts. Half the stage is dark and silent, and that is life; the other half is arc-lit, sparkling, loquacious, and that is the legend. If an individual strays from life to the legend, he is transfigured. Either he becomes a hero, radiant and wonderful, or a villain, louring and malignant. In the legend there are no men, only heroes and villains; in life there are no heroes or villains, only men. . . . Of course, there has always been this division between life and legend. It is merely that in our time greater facilities for dramatising it (literacy, radio, television, etc.) have become available. These facilities have not created the division. They have been invented to make it more manifest."—MALCOLM MUGGERIDGE, *New Statesman*, Aug. 17, 1957, p. 191.

DENTAL EXTRACTION IN HÆMOPHILIA

C. WISHART
B.D.S. Durh., F.D.S. R.C.S.
FORMERLY SENIOR DENTAL REGISTRAR, UNITED OXFORD HOSPITALS

C. ANNAND SMITH
L.D.S. R.C.S.E.
SENIOR HOSPITAL DENTAL OFFICER, UNITED OXFORD HOSPITALS

G. E. HONEY
B.M. Oxfd, M.R.C.P.
SENIOR MEDICAL REGISTRAR, UNITED OXFORD HOSPITALS

K. B. TAYLOR
D.M. Oxfd, M.R.C.P.
ASSISTANT TO NUFFIELD PROFESSOR OF CLINICAL MEDICINE

THE RADCLIFFE INFIRMARY, OXFORD

EXTRACTION of teeth from a patient with hæmophilia is an operation which most dental surgeons avoid. It is almost always followed by bleeding, which may persist for weeks. The amount of blood lost at the operation is usually not abnormal; but within a few hours bleeding recurs, and it may persist, so that large quantities of blood may be lost. The following two cases illustrate the results obtained before 1954.

The first was a severe hæmophiliac aged 43 [no. 6394]. He had eleven teeth removed in eight operations. These were done over the course of 10 years. Of this time, 139 days were spent in hospital and on 54 of these days he was bleeding from tooth sockets. In all he had 13 transfusions.

The second was aged 36, a severe hæmophiliac, from whom three teeth were removed, one at a time. He was given 17 separate transfusions, had 30 days' postoperative bleeding, and was in hospital 87 days [no. 32036].

Treatment, ideally, would correct the basic defect in blood coagulation: dental extractions could then be carried out as in a normal person. At present the only way of restoring the defective coagulation mechanism to an efficient level is the intravenous injection of the globulin fraction of plasma which contains the anti-hæmophilic factor (see Biggs 1957). Unfortunately, truly hæmostatic blood-levels of antihæmophilic globulin (A.H.G.) cannot be achieved without using concentrated animal or human A.H.G. (Macfarlane, Biggs, and Bidwell 1954, Kekwick and Wolf 1957) and the use of animal A.H.G. is now seldom justified for relatively minor procedures such as dental extractions. However, it has been found that bleeding after dental extractions can be reduced or occasionally prevented by the use of large transfusions of fresh plasma and the local application of well-fitting dental splints.

This communication describes such a technique and gives an account of the results obtained with it.

Method and Management

The patient is admitted to a medical ward for the whole of his treatment. The diagnosis of hæmophilia must be established by standard laboratory tests, and a general physical examination made in order to rule out the presence of disease which might make impracticable the rapid transfusion each day of one litre of human plasma. The teeth and jaws are X-rayed and any necessary pre-operative scaling of the teeth is carried out. Impressions of the mouth are taken, from which moulded splints of transparent acrylic resin are made to be fitted accurately over the empty sockets as soon as the teeth are removed. They serve two purposes: first, they allow gentle pressure to be exerted on the gum margin; and secondly, they prevent the clot, when formed, from being dislodged. There is a real value in making the splint transparent, for the underlying gum can then be seen through it, and reduces the risk of the splint being left too tight and so causing strangulation of the blood-supply to the mucous membrane, which would then ulcerate. These splints are made to be clasped to standing teeth; in cases requiring total clearance, four teeth, preferably premolars, must be retained in the first instance for this purpose. On the day of operation the patient is started on a course of penicillin orally (penicillin V 200 mg. every 6 hours). It is important to avoid intramuscular injections in the hæmophiliac because of the risk of producing a large and painful hæmatoma.

The operation itself is planned to take place at a definite time. An hour before this, an intravenous infusion is set up and the plasma from 4 pints of normal human blood transfused. It is important that the plasma be separated as soon as possible after the blood is shed and given to the patient at once. Recently, however, it has been found that plasma can be frozen and then stored at −30°C for several weeks without loss of antihæmophilic activity. When required, this frozen plasma can be thawed out. This is a great help in management because plasma can be stored in readiness for the treatment of each case. One litre of plasma is given and the rate of flow regulated so that the transfusion ends an hour later, just as the dental surgeon is removing the first tooth. It should be emphasised that rapid transfusion of plasma is essential if the A.H.G. in the patient's blood is to be raised to a hæmostatic level at the time of operation. General anæsthesia is used, given through an armoured endotracheal tube carefully passed through the mouth (Leatherdale 1957). Atropine gr. $^1/_{100}$ is given intravenously as premedication and light anæsthesia employed. The anæsthesia should be light so that the patient recovers consciousness before leaving the operating-theatre. He can then coöperate and if necessary exert gentle pressure on the bleeding surface through the splint.

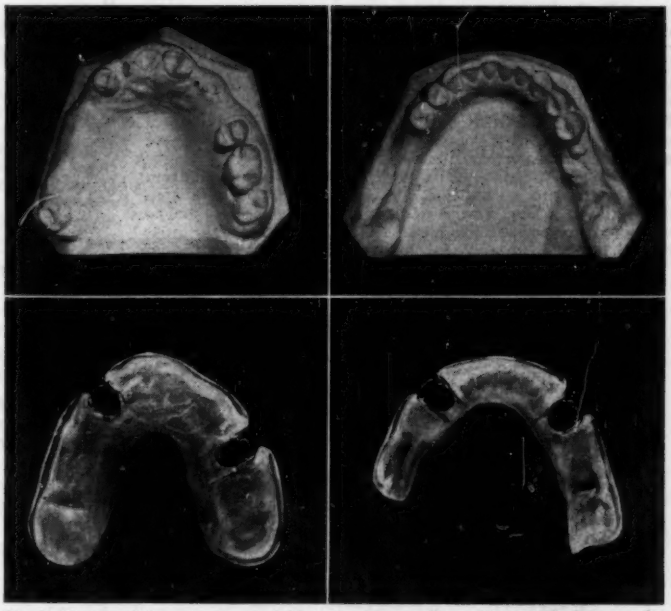


Fig. 1—Models of jaws (upper on left) and corresponding splints made for use after extraction of $\frac{87\ \ 21\ |\ 1\ 3\ 78}{765\ 321\ |\ 123\ 5}$, leaving R3 and L6 in upper jaw and R4 and L4 in lower jaw to provide an anchorage for the splints.

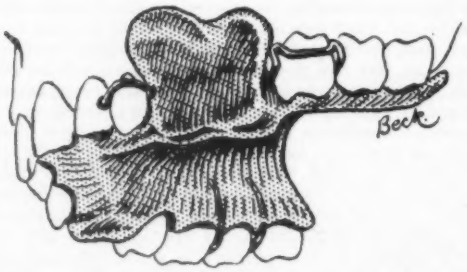


Fig. 2—Upper-jaw splint anchored firmly in situ, covering sockets of L4,5 and R4.

The teeth are extracted as carefully as possible and firm pressure is applied with the fingers to coapt the socket margins. The saddles of the acrylic splints are lined with a thin layer of calcium-alginate gauze soaked in Russell's viper venom and then firmly seated in position. They are left untouched for the next 7 days during which time a further transfusion of one litre of fresh or frozen plasma may be given daily or as required. At the end of this period the splints can usually be removed and the transfusions stopped without the risk of further bleeding. In those cases where four teeth are left as abutments, they are usually removed at a second operation similarly planned, 3–5 days after the first. In this event, transfusions of plasma may be required for a week after the second operation. Whilst the splints are in position, the patient can take a soft diet; but he should be warned not to disturb them.

Construction of the Splints

The splints should be designed so that they will remain comfortable and stable in the mouth and, if bleeding occurs, are capable of transmitting pressure to the underlying soft tissues when the jaws are clenched. Their function is to exert a gentle lateral pressure against the socket when required. Vertical pressure is to be avoided because it will evert the socket margins, and continuous pressure is undesirable because it will cause necrosis of the mucosa. The simplest type of splint, which is perfectly adequate for most cases, is made of clear acrylic resin and incorporates Adams's modification of the arrowhead crib for retention. These cribs have been chosen because they can be adapted for use in most parts of the mouth and ensure a very stable appliance. When the plate has been seated at operation to check for accuracy of fit, the tension of these cribs can easily be varied. Occlusal rests may be added to prevent excessive pressure on the wound edges during mastication.

Alginate impressions are taken in special trays, and from them master models are cast in hard plaster to be duplicated as required. The crowns of those teeth which are to be extracted are cut off the model, and the gingival margin is carved to the estimated contour of the alveolus. This should be done by the operator and not left to the technician, since the shape of the socket margin depends upon such variable factors as the periodontal condition, the size and shape of the roots, the density of the supporting bone, and the technique of extraction. The models are then carefully surveyed and all unnecessary undercuts eliminated before they are duplicated and mounted on an articulator in occlusion. The teeth opposing the splints are covered with a layer of sheet soft metal and the splints waxed up so that the upper and lower occlusal surfaces are in contact. This ensures that the splint will be free of the bite. The buccal and labial mucosa usually shows some postoperative œdema 2–3 days after extraction, which tends to produce ulceration from pressure of the splint. To avoid this, it has been found helpful to relieve the labial or buccal sulcus on the model at the peripheral margin of the splint, which itself should be thickened.

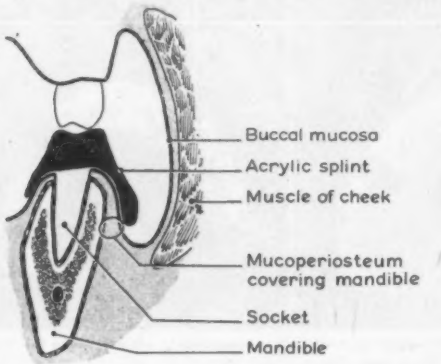


Fig. 3—Coronal section of mouth, showing a mandibular splint in position.

The retention of a splint to cover the last remaining sockets in either maxilla or mandible presents particular difficulties, since no abutment teeth remain. Modified Gunning-type splints may be used (Felix 1950), but their stability depends on complete coöperation from the patient. Better splinting of these upper sockets can be achieved by a simple acrylic-base plate incorporating extraoral arms which can be connected by rods and universal joints to a plaster headcap. In the case of the mandibular sockets, a spring-loaded splint has been used with success and is well tolerated by the patient.

Results

These techniques were developed over the course of 3 years. The use of fresh plasma transfusions before operation, without acrylic splints, did not much improve the postoperative course. With the introduction of acrylic splints our results have changed completely. Our experiences with this complete technique are shown in the table. Here the cases are divided into two separate groups. In the first group only a few teeth were removed at each operation, since we were not able to predict how effective our methods of achieving hæmostasis would be. Our experience with this first group of patients allowed us to draw certain firm conclusions. In the first eleven patients treated in this way it was clear that the method was successful, reducing the number of days of postoperative bleeding and expediting the rate of healing. However, experience with the twelfth patient suggested that a conservative policy might not be always in the best interests of the patient:

This patient was a man aged 26, with severe hæmophilia, who was admitted for a complete dental clearance, having still twenty-nine teeth. It was decided to proceed cautiously and his teeth were removed two, three, or four at a time. The postoperative course after the first three sets of extractions was uneventful and there was no significant bleeding. However, with subsequent extractions the hæmostatic response to fresh plasma diminished and postoperative bleeding gave more trouble, and his length of stay in hospital was very protracted.

Reviewing the first eleven cases it was clear that bleeding did not continue for a longer time if six teeth were removed rather than one or two. This observation, together with the apparent increasing resistance of case 12 to transfusion, suggested that it might be possible safely to remove more than six teeth at one session.

In the four cases whose treatment is recorded in the second part of the table, we therefore decided to proceed boldly and reduce the number of operations in each to two, leaving 3–5 days clear in between each operation. Case 14, a severe hæmophiliac, developed a circulating anticoagulant postoperatively and had to be treated with bovine A.H.G. In view of this it was decided not to remove the remaining four teeth but treat them conservatively.

In the other three cases the extractions were done without complications. One patient (no. 13) had troublesome bleeding for 24 hours and required a transfusion of seven pints of blood; but with the other two patients the postoperative bleeding was no more profuse than in those cases from whom fewer teeth had been removed.

Discussion

Our experiences incline us to the belief that it is reasonably safe to extract teeth in the adult hæmophiliac in numbers similar to those extracted in the normal subject in one operation. While we would agree with Orr and Douglas (1957) about the complete safety of a conservative policy of removing one or two teeth at a time, the length of stay in hospital with such a policy becomes excessively long and a burden both to the patient and his attendants. In our opinion more teeth may be removed, without undue risk, provided the patient is fully coöperative, and that he does not have in his blood a circulating anticoagulant, and also provided that concentrates of animal A.H.G. are available in emergencies such as that described in case 14.

Orr and Douglas have pointed out that the amount of blood-loss is proportional to the number of teeth removed at one operation; but in our experience the duration of bleeding is not, since healing in all areas proceeds pari passu. Blood-loss, in itself, if it does not continue for weeks, may even be an advantage, since it allows the rapid transfusion not only of fresh plasma but also of fresh blood. It cannot be claimed that a fully hæmostatic level of A.H.G. can be achieved in the patient's plasma by transfusions of either fresh blood or plasma; but the more is given, the more the bleeding tendency is reduced.

SUMMARY OF RESULTS

Part 1.—A cautious approach: not more than six teeth extracted at one session

Case	Severity of disease (Level of A.H.G.)	Age	No. of teeth and roots removed per operation	Complications	No. of transfusions	Total fluids transfused	Days of bleeding *	Days until healed (splints removed)
1. [215484]	Severe (nil)	42	(*a*) 2	Nil	1	2 pints plasma	Nil	7
			(*b*) 4	Nil	1	2 pints plasma	3	10
			(*c*) 3	Nil	1	2 pints plasma	Nil	7
2. [223822]	Moderate (9 %)	21	(*a*) 1	Nil	1	2 pints plasma	2	7
			(*b*) 6	Nil	2	3 pints plasma	3	6
3. [215060]	Moderate (5 %–7 %)	34	1	Recent acute abscess	Nil	Nil	Nil	6
4. [224764]	Mild (10 %–13 %)	24	(*a*) 4	Nil	1	2 pints plasma	2	6
			(*b*) 6	Nil	1	2 pints plasma	3	10
5. [206422]	Mild (4·5 %)	56	(*a*) 1	Nil	Nil	Nil	2	5
			(*b*) 1	Nil	1	2 pints plasma	3	8
			(*c*) 3	Parodontal abscess 7	2	4 pints plasma	6	8
6. [220019]	Severe (nil)	31	3	Infected teeth—difficult to remove	2	2 pints plasma 4 pints fresh blood	5	10
7. [67196]	Mild (5 %)	20	6	Resolving abscess	2	3 pints plasma 1 pint fresh blood	8	9
8. [216585]	Moderate (5 %)	56	(*a*) 2	Recent acute abscess	2	2 pints plasma 2 pints fresh blood 1 pint stored blood	7	11
			(*b*) 3	Nil	1	2 pints plasma	11	12
9. [179023]	Mild (25 %)	6	(*a*) 1	Nil	1	1 pint plasma	Nil	6
			(*b*) 1	Nil	Nil	Nil	Nil	4
10. [102140]	Severe (nil)	56	6	Nil	4	8 pints plasma † 2 pints fresh blood	Nil	6
11. [212995]	Severe (nil)	20	2	Nil	1	2 pints plasma	Nil	6
12. [217568]	Severe (nil)	26	(*a*) 4	Nil	1	2 pints plasma	3	8
			(*b*) 3	Some laceration	2	4 pints plasma	12	13
			(*c*) 2	Nil	2	2 pints plasma 1 pint fresh blood	5	7
			(*d*) 3	Difficult extractions. Splint removed and refitted	3	6 pints plasma 2 pints fresh blood	7	10
			(*e*) 3	Erosion of gum by splint	3	6 pints plasma	8	20
			(*f*) 5	Nil	5	10 pints plasma 2 pints fresh blood	11	15
			(*g*) 4	Nil	5	10 pints plasma	14	17
			(*h*) 5	Erosion of gum	6	9 pints plasma 4 pints fresh blood	8	18

Part 2.—A bolder policy: all extractions to be carried out in not more than two sessions

13. [735786]	Severe (nil)	32	(*a*) 16	Nil	10	18 pints plasma 4 pints fresh blood 3 pints packed cells	8	10
			(*b*) 3	Nil		(Under cover of above)		7
14. [237993] ‡	Severe (nil) + circulating anticoagulant	38	18	Nil from local causes	7	5 pints fresh plasma 2 pints fresh blood 3 pints stored blood 4 doses A.H.G. (bovine)	6	11
15. [90805]	Severe (nil)	23	(*a*) 6	Nil	2	4 pints plasma	3	4
			(*b*) 6	Laceration	3	4 pints plasma 2 pints fresh blood	10	12
16. [231932]	Moderate (5 %)	51	(*a*) 5 3 days apart	Nil	1	2 pints plasma	Nil	6
			(*b*) 7	Nil	1	2 pints plasma	4	10

* In "days of bleeding," we have included even slight oozing of blood from the sockets.
† Removal of teeth was carried out in conjunction with an operation for fenestration of a dental cyst. It was the latter which bled and for which blood-transfusion was required.
‡ This case is also referred to by Macfarlane et al. (1957) as case 8.

We believe that well-fitting splints are an essential factor in the technique we have described, and their making demands the utmost accuracy.

Finally, it must be stressed that full coöperation between patient, physician, dental surgeon, anæsthetist, pathologist, and blood-transfusion service is necessary to ensure maximum success.

Summary

A technique for the removal of teeth from hæmophiliacs is described. This involves the use of transfusions of fresh plasma and well-fitting acrylic dental splints. By these means, total extractions may be done in two operations without hazard to the patient, provided certain essential precautions are taken. These are described.

We wish to thank Prof. L. J. Witts and Dr. P. C. Mallam for permission to publish details of patients admitted under their care. Dr. Rosemary Biggs and Dr. R. G. Macfarlane have given constant advice and encouragement. Professor Witts very kindly read the typescript. This work would have been impossible without the invaluable coöperation of the Oxford Regional Blood Transfusion Service. The diagrams for figs. 2 and 3 were drawn by Miss Marjorie Beck.

REFERENCES

Biggs, R. (1957) *Lancet*, ii, 311.
Felix, P. (1950) *Brit. dent. J.* **88**, 32.
Kekwick, R. A., Wolf, P. (1957) *Lancet*, i, 647.
Leatherdale, R. A. L. (1957) *Anæsthesia* (in the press).
Macfarlane, R. G., Biggs, R., Bidwell, E. (1954) *Lancet*, i, 1316.
— Mallam, P. C., Witts, L. J., Bidwell, E., Biggs, R., Fraenkel, G. J., Honey, G. E., Taylor, K. B. (1957) *Ibid*, ii, 251.
Orr, J. A., Douglas, A. S. (1957) *Brit. med. J.* i, 1035.

LIPÆMIA, HEPARIN, AND BLOOD VISCOSITY

WILLIAM C. WATSON
M.B. Glasg., M.R.C.P., F.R.F.P.S.
ASSISTANT LECTURER IN MATERIA MEDICA AND THERAPEUTICS, GLASGOW UNIVERSITY; REGISTRAR, UNIVERSITY MEDICAL UNIT, STOBHILL GENERAL HOSPITAL

THE viscosity of a liquid may be increased by the addition of particulate matter. After a fatty meal particulate fat, in the form of chylomicrons, is added to the blood. It is important to know whether this postprandial lipæmia increases blood viscosity or not; for an increase in the viscosity of a liquid, other conditions being unchanged, diminishes its rate of flow. The implications of this in terms of in-vivo tendency to coagulation and tissue ischæmia are obvious.

I. Lipæmia and Viscosity of Plasma

Method and Results

For the purpose of this study the measurement of relative viscosity is adequate. A Hess's viscometer was used. After practice with the instrument and standardisation of technique, which included scrupulous care in cleaning, individual results rarely varied more than ±0·05. At first the mean of ten readings was taken, but this was found to be unnecessary and later only two or three readings were recorded. Lipæmia was measured as units of turbidity in an 'EEL' photometer using a red filter.

The subjects were convalescent patients of both sexes. Their ages ranged from 15 years to 78. Blood was withdrawn from an arm vein by a short wide-bore needle into a dry syringe. Samples were taken while the subjects were fasting and three hours after the ingestion of 50 g. cream fat. To obtain plasma samples, 8 ml. of blood was added to a small quantity of potassium oxalate (about 3 mg.), inverted gently five or six times, and spun at 3000 r.p.m. for ten minutes. Oxalate in this quantity has no effect on blood or plasma viscosity (Langstroth 1919). Serum samples were obtained by allowing the blood to clot and then centrifuging as for plasma. Hæmolysed samples were discarded.

TABLE I—SERUM AND PLASMA VISCOSITY READINGS IN THE FASTING STATE AND 3 HOURS AFTER INGESTING 50 G. OF CREAM FAT

		Turbidity		Viscosity	
		Fasting	3 hr.	Fasting	3 hr.
Serum readings (25 subjects 29 tests)	Mean ..	5·7	26·2	1·88	1·88
	Range ..	3–11	4–57	1·60–2·40	1·60–2·40
	Standard deviation	1·9	14·2	0·15	0·17
Plasma readings (21 subjects 23 tests)	Mean ..	5·7	38·5	2·01	2·04
	Range ..	3–7	15–78	1·75–2·25	1·75–2·35
	Standard deviation	1·5	13·5	0·17	0·13

Although the laboratory temperature varied between 14°C and 22°C during the period of the study, there was no significant variation in temperature while any group of comparative readings was being taken.

The results are shown in table I. The turbidity readings cover a clinically representative range of lipæmia. It is clear that serum and plasma viscosities were not affected by the presence of particulate fat in the concentrations encountered clinically. The slightly higher value of the mean plasma viscosity as compared to serum viscosity is in conformity with established knowledge (Wintrobe 1956).

Conclusion

Lipæmia of clinical degree has no effect on serum or plasma viscosity.

II. Lipæmia and Viscosity of Whole Blood

Although lipæmia has no effect on serum or plasma viscosity, it cannot be assumed that it will have no effect on the viscosity of whole blood. Nygaard et al. (1935) have shown that there is a linear relationship between blood viscosity and the hæmatocrit, for the hæmatocrit range of 15–50%. The particulate content of the blood also varies in respect of chylomicrons. If during lipæmia the increase in fat particles is sufficient, an increase in viscosity might occur. The aim of this part of the study was to examine this possibility and also to investigate the effect of heparin on blood viscosity in fasting and lipæmic subjects.

Method

The method and the subject sample were as before, except that:

(1) Viscosity readings were made at the bedside immediately after the blood was withdrawn. The four samples from each patient (see later) were allowed to stand at room-temperature until about 1–2 hours after the last one had been withdrawn, and their viscosities again measured in a group. It was not at first appreciated that this time interval was critical. The specimens were next centrifuged and plasma viscosities estimated.

(2) After withdrawing the 3-hour sample the needle was left in situ and 5000 units of heparin injected. Further samples were taken from the opposite arm 15 and 75 minutes later. For simplicity of reference, the fasting, 3-hour, and first and second post-heparin samples are called A, B, C, and D respectively. Readings taken after the samples had stood in vitro are indicated by the suffix "L." V = viscosity and T = turbidity, e.g.,

VAL = viscosity of fasting sample after standing at room-temperature.

The results of 21 experiments are shown in table II.

(3) Two samples of C were taken. One was centrifuged immediately for the estimation of plasma turbidity before

TABLE II—PLASMA-TURBIDITY AND BLOOD-VISCOSITY READINGS IN 21 SUBJECTS TO SHOW THE EFFECT OF LIPÆMIA, CLEARING ACTION OF HEPARIN, AND STANDING AT ROOM-TEMPERATURE FOR 1–2 HOURS

Case no.	Plasma turbidity				Blood viscosity							
					Bedside readings				Delayed readings			
	A	B	C	D	A	B	C	D	A_L	B_L	C_L	D_L
43	6	48	19	4	5·70	5·35	5·25	5·20	5·45	5·50	6·20	5·25
44	7	34	33	7	4·45	4·25	3·95	4·05	4·40	4·40	4·20	4·15
45	6	37	15	7	4·65	4·40	4·25	4·20	4·60	4·60	4·90	4·40
46	7	39	15	4	4·55	4·30	4·20	4·15	4·35	4·20	4·85	4·15
48	4	54	23	..	5·00	4·80	5·00	4·60	4·85	4·80	5·70	..
49	6	31	19	7	5·10	4·70	4·75	4·70	5·10	4·75	6·00	4·75
50	4	46	12	..	4·90	5·00	5·00	..	4·90	5·10	5·10	..
51	6	78	60	11	5·65	5·35	5·50	5·50	5·70	5·65	8·00	5·70
52	4	32	10	5	4·85	4·35	4·35	4·30	4·45	4·45	4·80	4·45
55	5	46	36	5	5·20	5·00	4·90	5·05	5·00	4·90	6·00	5·05
56	3	19	7	3	3·80	4·00	3·90	3·95	3·80	4·00	4·00	3·80
57	4	15	8	4	4·60	4·40	4·40	4·30	4·70	4·45	4·45	4·40
58	5	28	12	10	5·50	5·15	5·00	5·10	5·30	5·20	5·20	5·10
59	4	50	10	7	5·70	5·80	5·60	5·50	5·70	5·80	5·80	5·70
61	4	45	15	7	4·50	4·40	4·20	4·35	4·30	4·20	5·10	4·35
62	4	25	9	4	4·15	4·35	4·25	4·30	4·30	4·35	4·25	4·25
63	4	34	19	5	4·00	4·30	4·20	4·30	3·95	4·25	4·60	4·35
65	5	8	6	5	4·10	3·80	3·75	3·60	..	3·55	3·80	3·65
66	7	64	59	7	4·65	4·65	4·65	4·50	4·50	4·45	5·50	4·50
67	6	26	15	6	4·65	4·60	4·60	4·60	4·50	4·50	5·00	4·60
69	4	34	19	5	4·00	4·30	4·20	4·30	3·95	4·25	4·60	4·30
Mean	5	38	20	6	4·75	4·63	4·54	4·53	4·69	4·63	5·15	4·57

further " clearing " occurred due to the continuing in-vitro action of the heparin in the sample. The other was used for viscosity measurements. In this way possible alterations in viscosity induced by packing of the red cells in the centrifuge was avoided.

(4) In ten fasting subjects blood viscosity was measured before and 15 minutes after the intravenous injection of 5000 units of heparin, and the readings repeated about 2 hours later (table III).

Results

The bedside readings will reflect more closely the circulating viscosity and are considered first. There is a slight fall in the mean blood viscosity of the lipæmic samples ($0{\cdot}05>P>0{\cdot}02$). A further slight fall is found 15 minutes after the intravenous injection of heparin ($0{\cdot}02>P>0{\cdot}01$). If, however, a difference between readings of 0·20 or more can be considered significant, twelve showed a fall in the viscosity of the lipæmic sample, four showed a rise, and five were unaffected. Table II shows no obvious relation between the nature of the change in viscosity and the degree of lipæmia.

By the same arbitrary standard the intravenous injection of heparin was followed by a fall in three and a rise in one case, seventeen being unaffected. Heparin has also no effect on the blood viscosity of fasting subjects (table III). As one would expect, there was no change in the turbidity of fasting plasma after intravenous injection of heparin.

TABLE III—BLOOD VISCOSITY IN 10 FASTING SUBJECTS BEFORE AND 15 MINUTES AFTER 5000 UNITS OF INTRAVENOUS HEPARIN

Case no.	Blood viscosity			
	Immediate readings		2 hours later	
	Fasting	15 min.	Fasting	15 min.
47	3·80	3·70	3·70	3·60
48	5·40	5·40	5·20	5·15
53	3·65	3·75	3·60	3·70
54	5·20	5·10	5·00	4·90
59	5·30	5·20	5·20	5·25
61	4·40	4·40	4·25	4·35
63	4·15	4·05	4·05	4·00
64	4·45	4·30	4·25	4·10
65	4·70	4·70	4·50	4·50
68	5·20	5·20	5·20	5·20
Mean	4·62	4·58	4·50	4·48

When the immediate and delayed readings are compared the only significant difference is the striking increase in the viscosity of C_L. This increase must be due to some change in the red cells, for no increase was found in the plasma viscosity of these samples. It also seems to require the presence of lipid and heparin together, for it is not caused by lipæmia in an unheparined sample (compare VB and VB_L) nor by heparin in a lipid-free sample (compare immediate and delayed post-heparin viscosities in table III). It seems therefore that a heparin-lipid complex is formed which attaches itself to the red cells, presumably by the force of the heparin electronegative charge.

If this hypothesis is correct, where the dose of heparin is constant throughout, there should be some relation

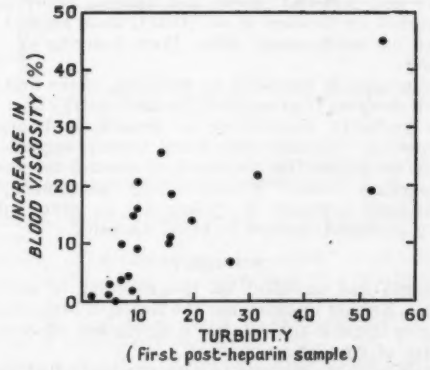


Fig. 1—Relation between the turbidity and in-vitro increase in viscosity of sample C.

between the percentage increase in VC on standing and its turbidity (i.e., between $\frac{VC_L - VC}{VC} \times 100$ and TC); for any increase in viscosity should depend to some extent on the amount of heparin-lipid complex formed. This relationship is plotted in fig. 1. There might have been closer correlation if the time-interval between VC and VC_L had been constant. In subject 67 the viscosity of the first post-heparin sample was measured at intervals, and in fig. 2 percentage increase in VC is plotted against time. The graph shows that the viscosity of this sample increases at a constant rate until some point just short of its maximum. Thus the degree of increase in VC seems to depend not only on the amount of heparin-lipid complex found but on the time allowed for it to combine with the red cells.

There is no increase in VD_L, presumably because the heparin-lipid complex has been cleared from the circulating blood during the intervening hour.

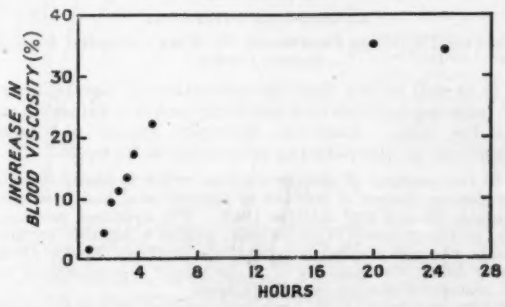


Fig. 2—In-vitro increase in viscosity of sample C plotted against time in one subject.

Discussion

It seems clear that postprandial lipæmia tends on the whole to diminish, rather than increase, blood viscosity. The difference is not gross, however, and is unlikely to have a significant effect on blood-flow.

It must be emphasised that these findings and conclusions apply, in a strict sense, only to the fixed physical conditions of the instrument used, and cannot be applied without reservations to the more complex problems of blood-flow in a system of tubes of varying calibre and elasticity (Fahraeus and Lindqvist 1931). Hence one cannot deduce that lipæmia has no effect on blood-flow in very narrow tubes such as capillaries and arterioles.

It also seems clear that heparin has no significant effect on blood viscosity in either the fasting or lipæmic subject. If heparin increases coronary flow volume, as reported by Gilbert and Nalefski (1949) and relieves effort angina as reported by Graham et al. (1951), these actions must depend on mechanisms other than lowering of blood viscosity.

The increase in viscosity, on standing, of the first post-heparin sample (VC_L) seems to be an in-vitro effect only. It is probably caused by a heparin-lipid-corpuscle combination. Swank and Levy (1952) suggest that heparin facilitates the transport of neutral fat through the capillary wall. Whatever the mechanism, this heparin-lipid complex is "cleared" in vivo without causing profound changes in blood viscosity.

Summary

Lipæmia has no effect on the viscosity of serum or plasma. Neither lipæmia, nor the action of heparin in the fasting or lipæmic subject, has a significant effect on the viscosity of circulating blood.

Certain in-vitro changes in viscosity are noted and an explanation for them is suggested.

I wish to thank Dr. J. W. Chambers for laboratory facilities at Stobhill General Hospital.

REFERENCES

Fahraeus, R., Lindqvist, T. (1931) *Amer. J. Physiol.* **96**, 562.
Gilbert, N. C., Nalefski, L. A. (1949) *J. Lab. clin. Med.* **34**, 797.
Graham, D. M., Lyon, T. P., Gofman, J. W., Jones, H. B., Yankley, A., Simonton, J., White, S. (1951) *Circulation*, **4**, 666.
Langstroth, L. (1919) *J. exp. Med.* **30**, 597.
Nygaard, K. K., Wilder, M., Berkson, J. (1935) *Amer. J. Physiol.* **114**, 128.
Swank, R. L., Levy, S. W. (1952) *Ibid*, **171**, 208.
Wintrobe, M. M. (1956) Clinical Haematology. London; p. 314.

USE OF GLUCOSE OXIDASE, PEROXIDASE, AND O-DIANISIDINE IN DETERMINATION OF BLOOD AND URINARY GLUCOSE

A. ST. G. HUGGETT
M.B., D.Sc., Ph.D. Lond.
PROFESSOR OF PHYSIOLOGY IN THE UNIVERSITY OF LONDON
D. A. NIXON
M.Sc. Lond.
LECTURER IN PHYSIOLOGY
From the Physiology Department, St. Mary's Hospital Medical School, London

IT is well known that the estimation of blood-glucose by reducing methods lack specificity and give values which are too high. Enzymes, however, enable a greater selectivity of the reducing substances to be made.

In the presence of glucose oxidase, which is highly specific for glucose, glucose is oxidised to gluconic acid and hydrogen peroxide (Keilin and Hartree 1948). The hydrogen peroxide can, in the presence of peroxidase, oxidise a suitable oxygen acceptor to give chromogenic oxidation products (Keston 1956, Teller 1956), the intensity of whose colour is proportional to the amount of glucose initially present.

White and Secor (1957) have demonstrated glucose on paper chromatograms by adding glucose oxidase and detecting the resultant gluconic acid by an acid-jodide-iodate-starch reaction, and the hydrogen peroxide by using peroxidase and an oxygen acceptor.

The method described here is based upon that of Teller (1956) and has been found suitable for extensive determinations of blood-glucose, particularly in the presence of fructose. Since it seems to be of value for both clinical and research purposes, the factors determining its accuracy deserve publication. A preliminary account has been published (Huggett and Nixon 1957a and b).

Method

Reagent

A mixed enzyme-oxygen acceptor reagent is prepared as follows:

Glucose oxidase 125 mg., peroxidase 0·5 mg., and 0·5 ml. of 1% o-dianisidine (in 95% ethanol) are taken and made up to 100 ml. with 0·5 M $NaH_2PO_4.2H_2O$ (adjusted to pH 7·0 with NaOH) and filtered through paper. This preparation is called here the reagent.

The sources of the enzymes, when not prepared from *Penicillin notatum* (glucose oxidase) or horse-radish (peroxidase), is important.

Glucose-oxidase preparations are obtainable from the Sigma Chemical Company, St. Louis, Missouri, U.S.A.; G. F. Boehringer and Soehne, G.M.B.H., Mannheim, Germany; and Takamine Chemical Company, New Jersey, U.S.A. The peroxidase is obtainable from Boehringer and from Nutritional Biochemical Corporation, Cleveland, U.S.A. A mixture of the two enzymes and oxygen acceptor is marketed in the U.S.A. under the proprietary name of 'Glucostat' by the Worthington Corporation, New Jersey, U.S.A. The work in this paper was done with the Sigma glucose oxidase and the Boehringer peroxidase.

The reagent may be stored in a brown glass bottle at −5°C with little loss of activity for about a week. It goes brownish owing to auto-oxidation of the o-dianisidine, but this colour is allowed for in the blank.

Anticoagulation and Inhibition of Glycolysis

Anticoagulation may be achieved either with heparin or with a mixture containing sodium fluoride 10 mg. and potassium oxalate 30 mg. per 10 ml. of blood (Bayliss 1950). The latter method is used where the prevention of glycolysis in stored blood is desirable. A tenfold increase in the concentration of this mixture is still without any effect on the efficiency of the reagent.

Deproteinising

Concordant results can be achieved using zinc, barium, or cadmium hydroxides or ethanol as deproteinising reagents.

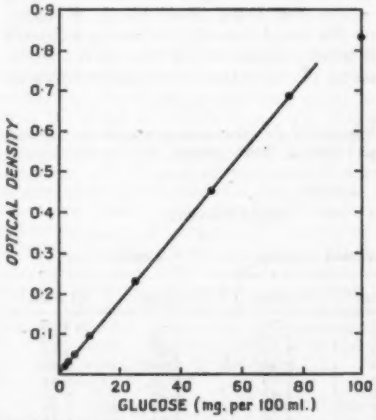


Fig. 1—The linear development of colour with increasing glucose concentrations in 0·1 ml. of glucose solutions and 2·5 ml. of reagent (read in 0·5-cm. cell after 60 minutes' incubation at 35°C).

Procedure

Whole blood.—It has been found convenient to use 0·2 ml. of a 1 : 10 deproteinised whole-blood filtrate. To this volume is added 2·5 ml. of the reagent. After 60 minutes' incubation in a water-bath thermostatically controlled at 35°–37°C the brownish-orange colour which develops is compared in a Spekker absorptiometer with 601 filters or in a Hilger spectrophotometer at 420 mμ with the colours produced

by a set of glucose standards at 5, 10, and 15 mg. per 100 ml. treated in the same manner.

In all cases the volume of the unknown filtrates and standard solutions and/or the volume of the reagent may be varied to produce a suitable depth of colour commensurate with the concentration of glucose expected.

Plasma.—Glucose may be estimated directly in plasma without deproteinisation by this method, the inherent colour of the plasma being allowed for by its inclusion in a blank with phosphate buffer or heat-inactivated reagent.

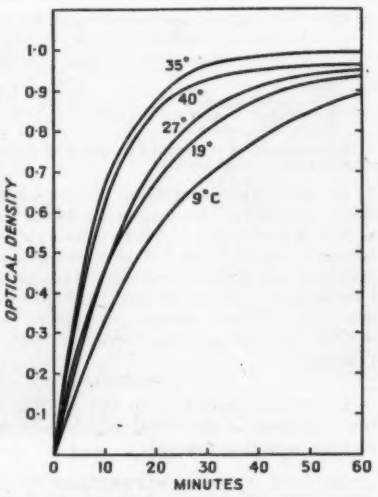


Fig. 2—Effects of different incubation temperatures on colour development in 0·1 ml. of 100 mg. per 100 ml. solution of glucose and 5 ml. of reagent (read in 1-cm. cell).

Urinary glucose.—Direct determination of glucose in fresh urine, with an appropriate blank, leads to poor recoveries. However, these difficulties may be overcome by first treating the urine with charcoal to decolorise it; a direct determination can then be made in the filtrate.

Results

Compliance with the Beer-Lambert Law.—The linear relationship of colour produced with increasing glucose concentrations is shown in fig. 1, the sensitivity being 1 μg. per 0·1 ml. By increasing the volume of the reagent to 10 ml. a straight-line relationship was obtained over the range 0–500 μg.

Variability.—The standard deviations of ten replicates with 10 and 25 μg. of glucose, expressed as a percentage of the mean, were 4·3% and 3·8% respectively.

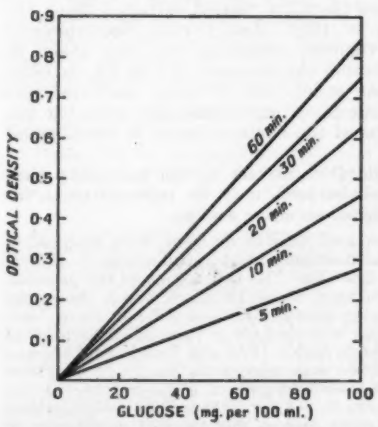


Fig. 3—Effects of different lengths of incubation at 30°C on development of colour, showing linear response in 0·1-ml. volumes of 25, 50, and 100 mg. per 100 ml. solutions of glucose with 5 ml. of reagent (read in 1-cm. cells).

Influence of incubation temperature.—With increased temperature there is an increase in the rate of colour development up to about 35°–37°C. The extent and rate of colour development decreased on incubation at higher temperatures owing to inactivation of the enzyme systems (fig. 2).

Influence of incubation time.—The linear relationship of developed colour with concentration is maintained at varying incubation times (fig. 3), maximum development being attained after 45–60 minutes.

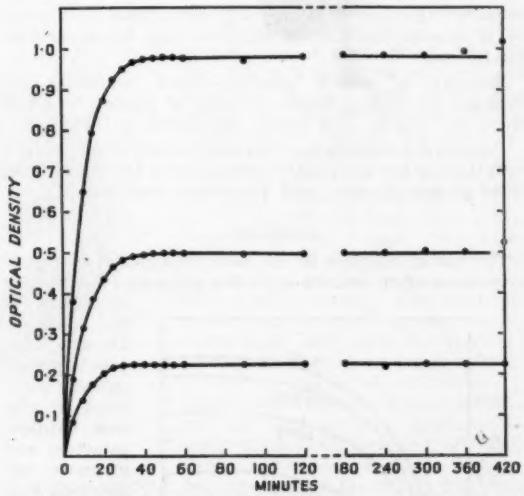


Fig. 4—Development and stability of colour of three different concentrations of glucose in 0·1-ml. glucose solutions with 5 ml. of reagent (read in 1-cm. cells after incubation at 35°C).

Stability of developed colour.—After 45–60 minutes' incubation the colour development is at a maximum and remains stable for about 5 hours (fig. 4). Accurate readings beyond this length of time cannot be made, because of progressive turbidity.

Influence of pH.—The system appears to have a pH optimum at 7·0, and a significant reduction in colour development is apparent when the pH value lies 0·5 of a unit either side of the optimum. The buffer contained in the reagent, however, has a high buffering capacity and can withstand the addition of acid or of alkali contained within the test solution under normal physiological conditions.

Optimum concentrations of glucose oxidase and peroxidase.—Increasing the concentration of glucose oxidase with a constant concentration of peroxidase increases the rate of colour development, but the degree of chromogenesis attained is reduced at high concentrations, possibly because of the presentation of the hydrogen peroxide to the peroxidase at a greater rate than it can utilise (fig. 5). In the presence of a constant concentration of glucose oxidase the optimum rate of colour development is given by 5·0 mg. of peroxidase (fig. 6).

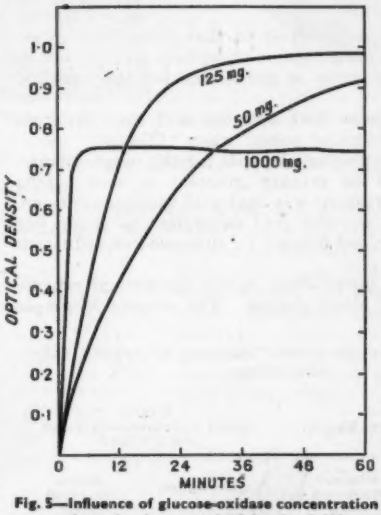


Fig. 5—Influence of glucose-oxidase concentration on colour development in 0·1 ml. of 100 mg. per 100 ml. solution of glucose and 5 ml. of reagent containing variable amounts of glucose oxidase in the presence of 5 mg. of peroxidase per 100 ml. of reagent (read in 1-cm. cells after incubation at 35°C).

However, this colour is only 5% more than that given by a reagent containing only 0·5 mg. of peroxidase per 100 ml.

Recovery of added glucose.—Good recoveries are obtained by adding known weights of glucose to whole blood and urine. The results are shown in table I.

Parallel determination.—The comparison of the method with three other methods commonly used for determining blood-glucose showed good agreement (see table II).

Discussion

The use of enzymes in the determination of biological substances often enables a greater accuracy, due to high specificity, to be achieved. Though glucose is preferentially oxidised by glucose oxidase, galactose and mannose are also attacked. However, the rate of reaction of these two hexoses, as judged by the development of colour with the reagent, is considerably slower than that of glucose. With equivalent concentrations the degree of chromogenesis given by galactose and mannose is only about 0·06% and 0·80% respectively of that given by glucose. The phosphate esters glucose-1-phosphate and glucose-6-phosphate do not serve as substrates for the enzymic reaction.

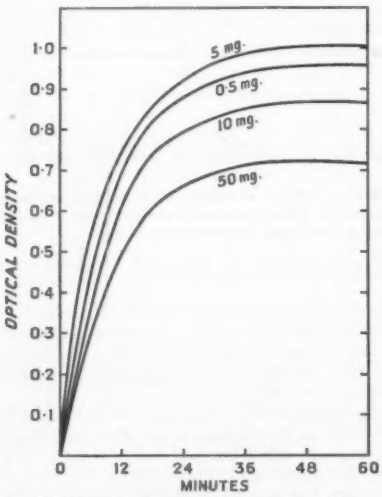


Fig. 6—Influence of peroxidase concentration on colour development in 0·1 ml. of 100 mg. per 100 ml. of solution of glucose and 5 ml. of reagent containing variable amounts of peroxidase in the presence of 125 mg. of glucose oxidase per 100 ml. of reagent (read in 1-cm. cells after incubation at 35°C).

Luntz (1957) notes that ascorbic acid may interfere with the development of colour when 'Clinistix' (commercial enzyme-impregnated paper for the rough quantitative assessment of urinary glucose) is used; but, when the present reagent was used with glucose solutions, concentrations of ascorbic acid equivalent to 5 mg. per 100 ml. of whole blood diluted 1 : 10 caused no reduction in chromogenesis.

The method is particularly suited for normal routine determinations of blood-glucose. The reagent is simple to prepare, and the method involves few operative steps. Since maximum chromogenesis takes place at 35°–37°C within 60 minutes and the colour is stable for several hours, accurate timing is unnecessary. When the assessment of the glucose concentration is urgent, a shorter incubation time can be used, but then accurate timing is essential. This is helped by adding 0·5 ml. of 0·05% sodium-cyanide solution, which inhibits further enzymic reaction.

TABLE I—RECOVERY OF ADDED GLUCOSE TO WHOLE BLOOD AND URINE

Whole blood (initial concentration 64 mg. per 100 ml.)		Urine (initial concentration 1 mg. per 100 ml.)	
Glucose added (mg.)	Glucose recovered (mg.)	Glucose added (mg.)	Glucose recovered (mg.)
3	4	1·2	1
3·5	5	7·4	5
10·6	13	17·1	17
20·8	20	33	34
38·4	35	82·9	80

TABLE II—PARALLEL DETERMINATION OF GLUCOSE IN WHOLE BLOOD BY REAGENT AND BY OTHER METHODS

Material = stored sheep blood.

	mg. per 100 ml.
Reagent	32
Hagedorn-Jensen	38
Somogyi colorimetric	33
Somogyi iodometric	35

The values cited represent the means of duplicate determinations of single samples of blood.

Summary

A method applicable to the routine determination of blood-glucose is described which uses a mixed enzyme-oxygen acceptor reagent.

REFERENCES

Bayliss, R. I. S. (1950) Practical Procedures in Clinical Medicine. London: p. 17.
Huggett, A. St. G., Nixon, D. A. (1957a) *Biochem. J.* **66**, 12P.
— — (1957b) *J. Physiol.* **137**, 3P.
Keilin, D., Hartree, E. F. (1948) *Biochem. J.* **42**, 230.
Keston, A. S. (1956) *Abstr. Amer. Chem. Soc.* 129th Meeting 31C.
Luntz, G. (1957) *Bril. med. J.* i, 499.
Teller, J. D. (1956) *Abstr. Amer. Chem. Soc.* 130th Meeting 69C.
White, L. M., Secor, G. E. (1957) *Science*, **125**, 495.

NEW METHOD OF STUDYING THE BACTERIAL FLORA OF INFECTED OPEN WOUNDS AND BURNS

R. H. GORRILL, M.D. Lond.
READER IN BACTERIOLOGY
E. J. K. PENIKETT, M.B. Lond.
LECTURER IN BACTERIOLOGY
GUY'S HOSPITAL MEDICAL SCHOOL, LONDON

INFECTION of wounds and burns in hospital is causing much concern (*Lancet* 1957). Published reports suggest that the incidence of hospital cross-infection has risen greatly in the past few years. Howe (1954, 1956) recorded an increase in postoperative wound infection from 1% in 1949 to 10% in 1954, mainly with *Staphylococcus aureus*. When vigorous measures had been taken to prevent cross-infection the incidence fell to 2% in 1955. As in most other series, the infecting bacteria were resistant to one or more antibiotics and reflected the resistance patterns of the bacteria found in the hospital environment.

There is considerable interest in the possibility that antibiotic-resistant bacteria may be more virulent for man than the original sensitive strains.

Rogers (1956) reported that in the New York Hospital in 1955 staphylococcal pneumonia had a case-mortality of 90% as against 30% in 1933–40. The average age of the patients, however, had risen from 36 to 53 years, which shows the difficulty of comparing mortality-rates at different times; and when the comparison was confined to cases of staphylococcal bacteræmia in children under 16 it was found that, whereas in 1940 this condition was responsible for 20–25 per 1000 admissions with a case-mortality of 37%, in 1949–55 the admissions were down to 2–4 per 1000 and the case-mortality to 20%. These figures suggest that there is no increase in virulence of staphylococci for patients of comparable age-groups.

With wound infection, where death is uncommon the virulence of organisms cannot readily be measured by statistical means; and there are as yet no satisfactory tests of virulence for the common infecting strains. But, though it has proved difficult to measure the virulence

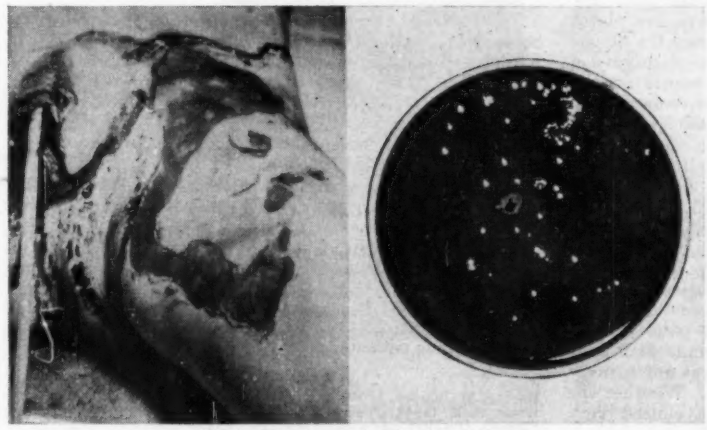


Fig. 1—Acute burn printed on blood-agar.

of bacteria for man by experimental infection (Elek 1956), study of the establishment and spread of a strain of bacteria in a wound or burn might give a valuable guide to its ability to establish infection.

The method we report here is extremely simple and based on the well-known replica plating technique of Lederberg and Lederberg (1952) which employs pads of sterile velvet to print bacteria from master plates on to plates containing special media. That technique has been extended by taking the initial print from the infected wound itself with a sterile velvet pad and using this pad to inoculate suitable ranges of selective media. By this means large areas can be sampled and one can see where each colony originated in the wound. From the plates prepared from the wound, replicates may be printed on a range of antibiotic media and the antibiotic resistance of all the colonies recorded.

Findings are much more informative with this method than where (as is usual) only a small sample is taken with a swab, and only representative cultures are taken for testing sensitivity to antibiotics.

Materials and Methods

Velvet Pads

Circles 3 in. in diameter are cut from rigid aluminium sheet. On one face a 4 in. rod of aluminium is fixed to serve as a handle. On the other face is stuck a disc of furnishing velvet.* The surface of the velvet is protected by covering it with a glass petri dish and the whole is wrapped in paper and sterilised in dry heat (160°C for one hour). Before using the pad, the paper is removed in the ward and the velvet inspected for damage or loosening from the plate through the petri dish. If satisfactory, it is lifted out of the dish and gently applied to the wound, care being taken to avoid slipping. The charged pad is then printed at once on suitable culture plates. The two difficulties encountered in the use of these discs have been the tendency of the fabric to come loose, and the change in texture of the velvet. It is important that the surface remains soft and free of caking, which occurs quite often. In fact the two difficulties have to some extent counteracted one another, because usually the velvet has come loose and had to be replaced before the surface was spoilt.

The primary plates may be printed on to antibiotic media, either using the discs described above or more conveniently by the use of sterile velvet squares stretched over a wooden block 3 in. in diameter. The squares of velvet are sterilised and stored in metal containers.

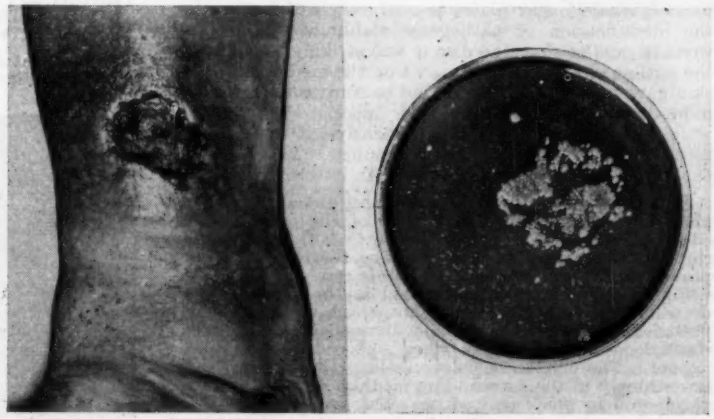


Fig. 3—Chronic varicose ulcer printed on blood-agar.

Media

In this particular investigation the media used were blood-agar, blood-agar containing 1 in 200,000 dilution of gentian-violet (gentian-violet plates), MacConkey-agar, and phenolphthalein-agar (Barber and Kuper 1951). Antibiotic sensitivity tests were done on suitable media containing known amounts of antibiotic, a convenient medium being that described by May and Morley (1952).

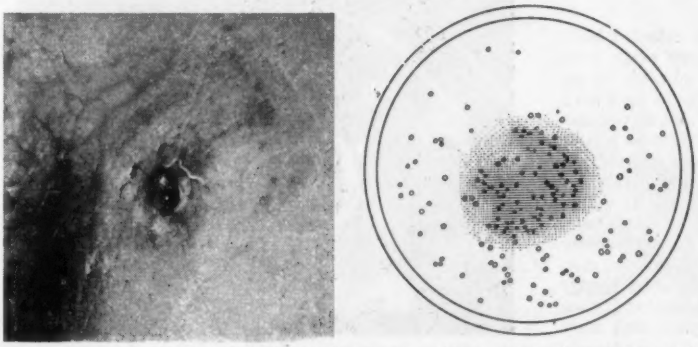


Fig. 2—Stitch abscess printed on phenolphthalein-agar. (Drawn from colour photograph.)

Results

Though we expected that prints taken by this method would yield only confluent growth, this seldom happened. More often the wounds yielded only a moderate growth, and the first problem was to decide how

* The adhesive used was 'Evo-stik,' made by Evode Ltd., Stafford, England.

many plates might be printed from the initial pad. By trial and error we found that almost always five plates could be used, and we made it the rule to print the blood-agar last, because we felt that unless this plate gave a satisfactory growth no reliance could be placed on the earlier more inhibitory plates. In order, the five used were: (1) phenolphthalein-agar to differentiate pathogenic from non-pathogenic staphylococci; (2) gentian-violet blood-agar for streptococci; (3) MacConkey medium for coliforms, &c.; (4) anaerobic blood-agar for clostridia and also because it was a useful control of plate 3 as a selective medium for hæmolytic streptococci; and (5) the control blood-agar. It is by no means certain that this is the ideal combination of plates and possibly it would be worth replacing one or more by antibiotic-containing media.

When it was realised that dry pads gave only a moderate number of colonies, tests were made with pads soaked in sterile broth; but this process was not entirely satisfactory and was not used extensively. Whether the pads were dry or wet, their application caused very little discomfort to patients.

The method was tested not only on burns, on infected operation wounds but also (very successfully) on chronic ulcers, especially varicose ulcers.

Value

Once the method was established, the printing of the primary plates on to the antibiotic media was as quick as the ordinary process of sensitivity testing. The phenolphthalein-agar plates proved very satisfactory in the identification of pathogenic staphylococci. With wounds smaller than the disc it was striking to see how the outline of the lesion appeared on the media. Normal skin gave only a few colonies and so contrasted with the more heavily infected wound or ulcer. With burns, which were usually much more extensive, it was helpful to include the skin edge when sampling. This allowed the plates to be orientated when examined next day.

Fig. 1 shows a child with severe burns and a blood-agar plate printed from the lower edge of the lesion. The edge runs across the plate from top to bottom: on the right is the normal skin flora and on the left coagulase positive staphylococci and *Escherichia coli*.

Fig. 2 shows an infected wound in the groin with a drawing made from a colour photograph of the phenolphthalein-agar plate. On this medium coagulase-positive staphylococci turn colour when exposed to ammonia vapour. The change in colour seen in the colonies and less strongly in the surrounding medium does not photograph well in black and white. The drawing has been included to show the contrast between the wound flora and the surrounding skin flora.

Fig. 3 shows the flora of a typical varicose ulcer seen on a blood-agar plate. It is a mixture of staphylococci, *Esch. coli*, and *Pseudomonas pyocyanea*.

Records of the wounds and the bacterial flora may be kept by taking colour photographs.

Failure

This method was of little use in wounds infected with *Proteus vulgaris*, for only on the MacConkey plate were discrete colonies seen. Deep wounds, very chronic ulcers with hard rings of scar tissue, and wounds in awkward sites did not print very well. Wounds allowed to become very wet with maceration of surrounding skin no longer showed the clear outline of the wound when printed.

If the position of a wound makes it unsuitable for printing, the second part of this method is still of value. Once the antibiotic sensitivity-testing plates have been prepared, it is as easy to test the whole culture by printing as to test single colonies by the more common procedures. Simple phage-typing can be done by spraying an aerosol of phage on the printed plate and then incubating. Sensitive colonies will be lysed and only resistant ones will grow (Beale 1948).

Conclusions

The bacterial flora of infected wounds can conveniently be sampled with velvet pads mounted on metal discs. A number of different media may be inoculated from a single pad. When the cultures have incubated, further study (e.g., antibiotic resistance) may be done by means of replica plating.

In many cases this method allows study of the wound flora as a whole. The distribution of bacteria (by position, type, and antibiotic resistance) can be recorded, the change in wound flora watched, and the importance of various strains of bacteria assessed.

As a research method it should help in the study of infection and healing in experimental wounds and burns.

We wish to thank the consultant staff of Guy's Hospital for allowing us access to their cases, and nurses for their help. We are indebted to the medical illustration department for photographing patients and cultures.

REFERENCES

Barber, M., Kuper, S. W. A. (1951) *J. Path. Bact.* **63**, 65.
Beale, G. H. (1948) *J. gen. Microbiol.* **2**, 131.
Elek, S. D. (1956) *Ann. N. York Acad. Sci.* **65**, 85.
Howe, C. W. (1954) *New Engl. J. Med.* **251**, 411.
— (1956) *Ann. N. York Acad. Sci.* **65**, 189.
Lancet (1957) i, 723.
Lederberg, J., Lederberg, E. M. (1952) *J. Bact.* **63**, 399.
May, J. R., Morley, C. W. (1952) *Lancet*, i, 636.
Rogers, D. E. (1956) *Ann. intern. Med.* **45**, 748.

New Inventions

TRACHEOSTOMY TUBE AND CONNECTIONS FOR PATIENTS HAVING INTERMITTENT POSITIVE-PRESSURE RESPIRATION

THE apparatus illustrated (fig. 1) overcomes most of the disadvantages of standard sets.

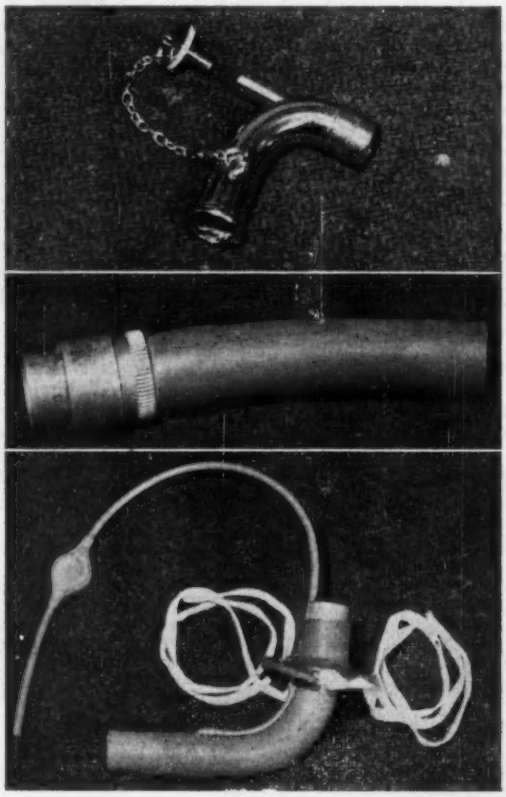


Fig. 1.

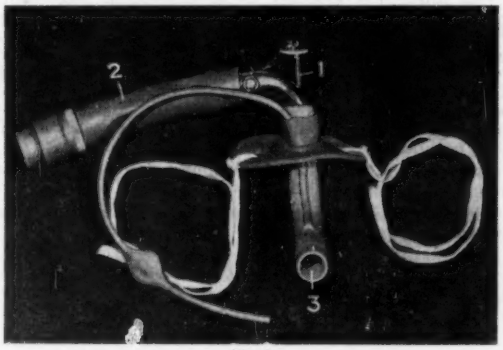


Fig. 2.

These include (1) difficulties with fixation to the neck, angulation, and drag; (2) loss of pressure and thus of pulmonary ventilation during tracheo-bronchial suction, causing partial asphyxiation of the patient; (3) excessive resistance in the connections, causing delay in emptying the lungs during the expiratory phase, with consequent rise in mean intrathoracic pressure, interference with venous return, and reduction in cardiac output; and (4) inability to allow for variation in the amount of subcutaneous tissue in the necks of different patients (in thin subjects the tube may press against the posterior tracheal wall causing ulceration, and in the obese the tube may only just enter the trachea, so that the cuff bulges into the tracheostomy wound [1]).

The metal connection with suction-piece (1; fig. 2).—The main feature of this is the suction-piece, which is made so that it exactly takes a size 6 E.G. suction catheter, and there is no loss of pressure or ventilation during suction. Size 6 E.G. was chosen as convenient for general use, but other sizes can be made up. The curve is smooth, and the angle is slightly over 90° to minimise angulation. Various sizes are available; the one illustrated fits a no. 12 endotracheal tube, intended for adult males, and is rather larger than the largest moulded rubber (Morrant-Baker) tracheostomy tube (42 F.G.), with consequent reduction in resistance.

The adapter (*catheter mount*) (2).—The metal part is of light alloy to minimise drag. It is half the weight of a standard piece, and is bored out inside to prevent turbulence. The rubber tube is of $^1/_2$ in. diameter.

The cuffed tube (3).—This is a portion of no. 12 endotracheal tube, curved to 90°, with a small built-in cuff with lead and pilot balloon. It has an adjustable collar to suit different types of patient. It will serve for several months. Smaller sizes are available.

A feature of the whole set is that the resistance to airflows used in intermittent positive-pressure respiration (30–60 litres a minute) is only 0·5–1·0 cm. water. There is five times this resistance in some standard sets.

The sets have been used at Rush Green Hospital, Romford, the Brook Hospital, Woolwich, and Joyce Green Hospital, Dartford, all of which are regional centres for the treatment of paralytic poliomyelitis.

The metal connection was made to my specification last year by Blease Anæsthetic Equipment Ltd., 12, Hinde Street, W.1, and its advantages would apply also to thoracic anæsthesia. The adapter was made for me by Messrs. Chas. King, 27, Devonshire Street, W.1, and can of course be used in anæsthesia. The tracheostomy tube was supplied by the British Oxygen Company, to the design of Dr. E. James of Rush Green Hospital, Romford, Essex.

JOHN BULLOUGH
M.B. Lond., F.F.A. R.C.S.

1. Noted also by J. M. K. Spalding and A. Crampton-Smith. *Lancet*, 1956, ii, 1247.

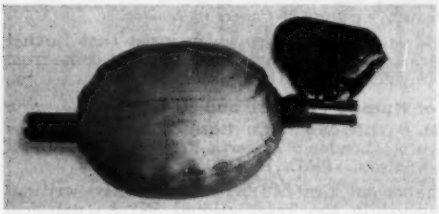
APPARATUS FOR RESUSCITATION AND SUCTION

THE two devices described here make it possible to treat efficiently, outside the operating-room and even in "the field," respiratory emergencies and unconscious patients. Anæsthesia thus becomes possible even in very primitive circumstances.

RESUSCITATION

There is a clear need for a resuscitation apparatus which does not rely on a supply of oxygen. Those hitherto described—e.g., the Oxford inflating bellows,[1] —depend on the bellows type of bag, which is clumsy, heavy, and tiring in continued use. The apparatus described here provides ventilation by the bag-and-mask method independently of cylinders and consists of a light, highly efficient, non-return valve and a self-expanding bag of conventional shape and texture (fig. 1).

1. Macintosh, R. R. *Brit. med. J.* 1953, ii, 202.



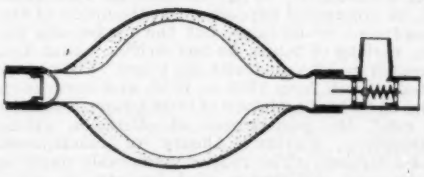
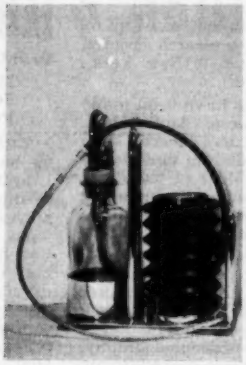


Fig. 1.

The bag is made of latex rubber and is lined with 'Sorbo' sponge-rubber, thicker at the poles, which acts as an expanding "spring," filling the bag automatically with air through a non-return valve at the opposite pole to the mask-mounting. It has a high filling-rate, making it possible to hyperventilate if necessary. The bag is connected to the mask-mounting and has a non-return valve of high efficiency and extremely low expiratory resistance (2 mm. H_2O at 50 litres flow per min.).

By interposing a piece of rubber tubing about 4 ft. long between the mask and the bag one can operate the resuscitator by foot, leaving both hands free to keep the mask airtight and the jaw forward. This, together with the high inflation capacity of the bag, may be advantageous to rescuers not used to keeping a face-mask in position.

The apparatus can be connected to an endotracheal tube connection or to a tracheotomy tube. The



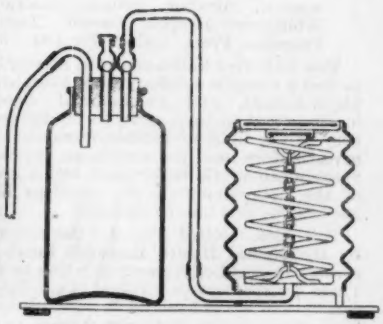


Fig. 2.

resuscitator can therefore be used to ventilate patients during anæsthesia; it has been used thus for more than 8 hours on several occasions. It may also be used for emergency treatment of patients with poliomyelitis and respiratory paralysis.

Where oxygen-enriched air is of advantage to the patient, a special bag has been constructed, which, apart from the tail-valve, has another valve through which additional oxygen can be run into the bag.

SUCTION

The apparatus shown in fig. 2 will work in an emergency even if it has not been maintained properly—e.g., has been left uncleaned after use or after long storage. It will work even if the suction bottle is full. These features are of special importance because suction is often needed in an emergency. In major catastrophes it is obviously an advantage to be independent of cylinders, water pressure, and electrical mains.

The apparatus consists of a concertina bag which causes suction by expanding. It is placed on the ground or the floor, and worked by intermittently compressing the bag with the foot. The apparatus continues to work if the suction bottle becomes filled. The valves are made of non-corrosive material and are large enough to let secretions and blood pass through. Even if secretions have been allowed to dry in the apparatus, it will still work because a spare valve is incorporated in it.

The bag can be cleaned without taking it to pieces, merely by pumping solutions through it.

The two apparatuses may be obtained from the British Oxygen Company Ltd.

HENNING RUBEN
CAND. MED. Copenhagen
Director, Department of Anæsthesia

ARNE RUBEN
MED. LIC. Stockholm

Finseninstitutet, Copenhagen

Reviews of Books

The Quicksilver Doctor

KENNETH DEWHURST. Bristol: John Wright & Sons. 1957. Pp. 192. 21*s*.

THIS is an account of the life and times of Thomas Dover, physician and adventurer. The powder which still bears his name has been a household remedy for two centuries; and the voyage round the world in which he played a conspicuous part was the most successful privateering expedition in British maritime history. It was during this voyage that Dover rescued Alexander Selkirk who, it is said, provided Defoe with the germ of truth which he swelled into the great romance of Robinson Crusoe. He met many famous contemporaries, amongst whom were Dr. Thomas Sydenham and Sir Hans Sloane.

This entertaining biography contains much new material. Dover had a varied and exciting life apart from his privateering voyage. As a physician in London he was known as the "Quicksilver Doctor," because of his liberal advocacy of crude mercury as a therapeutic aid. His famous grandiloquently titled book *An Ancient Physician's Legacy to his Country* was one of the more controversial medical books of the 18th century. He was involved in disputes with both the College of Physicians and the Company of Apothecaries.

But the real interest centres in Dover's voyage round the world, with its capture of prize ships and its attack on Spanish colonial towns for the sole purpose of holding them to ransom. The author delights in his hero and tells his story well, but few readers will agree with his statement: "The expedition to the South Seas which Dr. Thomas Dover helped to finance, and in which he was destined to play a leading role, was in no sense a buccaneering adventure or a piratical cruise. Adventure there was in abundance; but neither the origin, nature, nor exploits of this voyage could be described as piracy."

The story is set against the contemporary background, including an account of Dr. Mead's duel fought in the forecourt of the College of Physicians.

Schizophrenia

Somatic Aspects. Editor: DEREK RICHTER, M.A., PH.D., M.R.C.S., director, neuropsychiatric research centre, Whitchurch Hospital, Cardiff. London & New York: Pergamon Press. 1957. Pp. 180. 50*s*.

FOR well over half a century, attempts have been made to find a somatic ætiology for schizophrenia. Anatomical, physiological, and biochemical disorders have been incriminated in turn, only to be discarded as unsatisfactory in the light of further research. Most of the early investigators used too simple an approach, but in recent years more subtle techniques and a greater appreciation of the complexity of the problem have given a new impetus to this line of research.

This book resulted from a "discussion party" sponsored by the Mental Health Research Fund. Each contributor reviews the field of research in which he is actively engaged. There are chapters on physical characteristics, interaction of genetic and environmental factors, electro-encephalography, biochemical aspects, endocrine changes, pathological anatomy, consciousness and adaptive behaviour, metabolism, and drug action. Each chapter starts with a brief historical introduction, continues with a survey of the recent literature, with special emphasis on the author's own research, and concludes with an assessment of the present position.

Each contributor gives a clear and concise picture of the state of present research, with suggestions for profitable lines of future investigation. There are a number of omissions but, as Dr. Richter indicates in his introduction, the volume is not intended to be comprehensive. It should nevertheless prove an invaluable aid in absorbing the abundant writings on this very important aspect of mental disease.

Human Cancer

A Manual for Students and Physicians. MAURICE M. BLACK, M.D., associate professor of pathology, New York Medical College; FRANCIS D. SPEER, M.D., F.C.A.P., professor and director, department of pathology and clinical pathology, New York Medical College. Chicago: Year Book Publishers. London: Interscience Publishers. 1957. Pp. 273. 57*s*.

MUCH useful information, clinical experience, and wisdom are packed into this small volume, written as a guide to the problems of human cancer for medical students and practitioners.

Chapters on detection, including descriptions and discussions of laboratory tests, on human carcinogenic agents, both exogenous and possible endogenous ones, on the natural behaviour of tumours and biochemistry of cancer, and on current forms of treatment precede systematic descriptions of cancer in individual organs. The latter include tumours in childhood and functional growths of endocrine glands. Tumours of the nervous system of adults are omitted. Where it is immediately relevant to the human problem experimental work is clearly explained. Each chapter has a representative list of references, which extend to 1956. Figures given for incidence in various organs at different ages and by sex are derived from the report *Cancer in Connecticut 1935–51* and may be compared with our own Registrar-General's figures and with Harnett's *Survey of Cancer in London*.

Dr. Black and Dr. Speer cogently insist that further critical information about human cancer must come from practising physicians and their patients.

Problems of Human Pleasure and Behaviour

MICHAEL BALINT, M.D., PH.D., M.SC. Edited by ERNEST JONES, M.D. London: Hogarth Press and Institute of Psycho-Analysis. 1957. Pp. 300. 25*s*.

THIS is the second sheaf of Dr. Balint's fugitive writings to be published in the International Psychoanalytical Library. As is customary in psycho-analytic collections of this kind, no connected exposition is attempted of the author's standpoint or findings, but the reader can see what a wide variety of topics he has written about and how his approach has changed with the years. The papers here reprinted stretch from 1923 to 1956, and cover such diverse topics as "the dissolution of object-representation in modern art," the punishment of offenders, extra-sensory perception, Pavlov's theory of conditioned reflexes, and fetishism. The most considerable paper is that on individual differences of behaviour in early infancy.

Eskacillin

Children are available in three sizes—

little, middling, and big

'Eskacillin' is available in three strengths—100, 200, and 300.

If you match the strength of 'Eskacillin' to the size of the child you can prescribe simply 2 standard medical teaspoonfuls t.i.d.

Very simple. Kid's stuff, really.

under 8 Eskacillin 100
8 – 14 Eskacillin 200
over 14 Eskacillin 300
} 2 tsp. t.i.d.

the children's penicillin

Smith Kline & French Laboratories Ltd. Coldharbour Lane, London SE5

EC:PA157

THIS SUMMER TREAT FUNGAL INFECTIONS WITH TEOQUIL

The introduction of Teoquil, a new synthetic anti-fungal substance of low toxicity, marks a decided advance in the treatment of fungal infections of the skin.

Teoquil, in low concentrations, possesses a high degree of activity against mycelial fungi and some activity against yeast-like forms. It has also antibacterial properties which are particularly marked against Gram-positive organisms, including *Staphylococcus aureus*, *Staphylococcus albus* and *Streptococcus hæmolyticus*.

Teoquil is available in two forms—Teoquil Gel and Teoquil Dusting Powder. Teoquil Gel does not stain the skin or clothing. It may be used alone or in conjunction with the Dusting Powder in the treatment of fungal infections of the skin including Athlete's foot and tinea infections in other parts of the body.

TEOQUIL
TRADE MARK

Teoquil Gel is supplied in bottles containing 28 c.c., with brush.

Teoquil Dusting Powder is supplied in polythene 'puffer' bottles containing 25 grammes.

C57/309-10/H

ALLEN & HANBURYS LTD · LONDON · E·2
TELEPHONE: BISHOPSGATE 3201 (12 LINES). TELEGRAMS: "GREENBURYS, BETH, LONDON"

THE LANCET

LONDON: SATURDAY, AUGUST 24, 1957

Prevention of Maternal Deaths

THAT childbirth is far safer now than it was twenty years ago is well known. The extent of the improvement is evident from the maternal mortality: whereas in 1934 there were 2880 maternal deaths in England and Wales, in 1954 there were only 480. Almost as remarkable as the reduction in numbers has been the alteration in the causes of death. In the 1932 report by the Departmental Committee on Maternal Mortality and Morbidity, sepsis accounted for 37% of the deaths directly due to pregnancy and childbirth, compared with 3·8% in a report [1] on the years 1952–54. The chief causes of death in these years are given as toxæmia (including toxæmic accidental hæmorrhage) 22%, hæmorrhage (excluding toxæmic accidental hæmorrhage) 17%, abortion 14%, and pulmonary embolism 13%. But in one important respect the latest report shows little improvement over the position in 1934; at that time 45% of maternal deaths were considered to have a "primary avoidable factor," while in 1952–54 avoidable factors were still present in 43% of all deaths directly due to pregnancy and childbirth. Of deaths due to toxæmia of pregnancy (at present the principal cause of loss of a mother's life) 52% were found to be associated with avoidable factors; while of deaths due to hæmorrhage (the second commonest cause) 64% were associated with avoidable factors. It is a sobering thought that of 53 deaths due to retained placenta and post-partum hæmorrhage no less than 47 were associated with avoidable factors. Most of the deaths from pulmonary embolism were regarded as unavoidable. Two-thirds of the deaths due to abortion were regarded as avoidable, but the "avoidability" lay almost always in the fact that the abortion had been procured for non-therapeutic reasons. Avoidable factors were found in a third of the deaths from heart-disease—the principal cause of deaths classed as associated with pregnancy and childbirth.

Despite the enormous increase in the amount of antenatal care, the greatest source of error was inefficient or insufficient antenatal supervision; and this was especially evident in deaths from toxæmia of pregnancy. Some of these deaths were due to lack of integration between doctor, midwife, hospital, and clinic; and others were due to the patient's failure or refusal to seek advice. In considering hæmorrhage, the report states that the method of classification tends to minimise the importance of this factor. In deaths from hæmorrhage avoidable factors were especially frequent, the commonest error being failure to make proper use of obstetric flying-squads, which were called either too late or not at all. Attention is again drawn to the danger of moving a patient to hospital without resuscitation, or with the placenta undelivered—circumstances in which the value of the flying-squad has been amply demonstrated. The report suggests that such emergency units should not be staffed by juniors but that an experienced obstetrician should always be a member of the team. It could be added that an able anæsthetist should be present whenever a general anæsthetic is required, in view of the serious risk of inhalation of vomit: this accounted for 32 of the 49 deaths due to the complications of anæsthesia considered in the report.

In the opinion of the assessors the largest absolute number of errors was contributed by the domiciliary services. The main responsibility for referring high-risk cases to hospital, and therefore perhaps the greatest opportunity for error, rests with the domiciliary services; and the instances cited in the report make it clear that many doctors and midwives do not yet appreciate when a materially increased risk to the mother is present. Thus, from the total of 121 maternal deaths due to heart-disease, 33 confinements had been arranged outside hospital, and more than a third of the total did not receive hospital care or received it too late. Other examples of patients accepted for delivery outside hospital with fatal results are women of very high parity and women with a previous history of abnormalities of the third stage of labour. If an abnormality in the history or examination is discovered antenatally, the patient should be confined in hospital if at all possible; similarly when abnormality develops in an otherwise normal patient consultant advice should be sought promptly—especially if a short period of treatment at home has brought little improvement. The report indicates several instances of no action being taken when blood-pressure readings of over 160 mm. Hg systolic and 100 mm. diastolic with heavy albuminuria were observed for several days, or even weeks; hospital clinics have not always been blameless in this respect. Nothing in the report suggests that all women should be confined in hospital, but there is evidence on almost every page that only patients who are normal and who are not in the increased-risk group should be confined at home. Attention is drawn to the increased risk run by women over 35 years of age, by primiparæ over 30 years, by women who have borne four or more children, by patients with multiple pregnancies, and by patients in whom some abnormality is present or was present in a previous pregnancy.

The report suggests that maternal mortality may be further reduced by: (1) better antenatal care, especially in the early detection and early treatment of toxæmia; (2) prompter and more efficient treatment of hæmorrhage, especially through the use of flying-squads for emergency and domiciliary midwifery; and (3) better selection of cases for specialist care in hospital, especially women in the older age-groups and higher parities. Until more is learned about such important killing diseases as pregnancy toxæmia and pulmonary embolism, reduction of maternal deaths will depend mostly on better care of patients by individual doctors and midwives.

1. Report on Confidential Enquiries into Maternal Deaths in England and Wales, 1952–1954. H.M. Stationery Office, 1957. Pp. 60. 3s. 6d.

Control of Hæmophilic Bleeding

HÆMOPHILIC patients bleed because they have inherited a deficiency of a globulin factor essential for proper blood-clotting. The factor, for which the name "antihæmophilic globulin" (A.H.G.) is being increasingly used, is essential for the proper formation of plasma thromboplastin; without it prothrombin is hardly converted at all to thrombin, and so the fibrinogen of the plasma is imperfectly converted to fibrin. Christmas disease, which is clinically indistinguishable from classical hæmophilia, is due to the congenital absence of a different factor which, like antihæmophilic globulin, is essential for the formation of plasma thromboplastin. The Christmas factor, unlike antihæmophilic globulin, is not consumed in the clotting-reaction, and a useful source of Christmas factor is therefore blood-serum. Antihæmophilic globulin, on the other hand, is found only in normal plasma, and unfortunately when plasma is stored under usual conditions its antihæmophilic activity declines to zero within forty-eight hours. Hæmophilic bleeding can be controlled if enough antihæmophilic globulin can be obtained to ensure an effective level of antihæmophilic globulin for a sufficiently long period. In Christmas disease, the Christmas factor is needed and can be provided from stored plasma or serum, but since 9 out of 10 patients with clinical hæmophilia have classical A.H.G.-deficiency, the problem is largely one of providing antihæmophilic globulin. This problem has proved surprisingly difficult to solve, and earlier this year we commented [1] on it and on the valuable contribution of KEKWICK and WOLF [2] who had prepared an effective concentrate of human antihæmophilic globulin. This month we have published a series of papers from Oxford which illustrate progress in work on the control of hæmophilic bleeding. The authors of these papers do not propose any revolutionary new techniques, and similar methods are used by others; but their reports make it clear that with careful attention to detail it is now possible to control most hæmophilic bleeding and to undertake minor operations, such as dental extraction, with confidence, and, if absolutely necessary, major operations with some hope of success.

A first essential is to be able to estimate the level of antihæmophilic globulin in the blood. Only in this way can we judge the severity of a case, and whether an injection of A.H.G. has raised the blood-level sufficiently. Several methods have been proposed, but they have all been difficult to carry out away from specialised laboratories; Dr. BIGGS last week [3] proposed a technique which she hopes will be easier to use. Experience with this method has shown two things: firstly, that patients with severe clinical hæmophilia have a blood-A.H.G. level of 1% or less of normal, but in mild cases levels of up to 30% of normal may be found; and secondly, that if the A.H.G. level can be raised to over 30% of average normal before an operation, excessive bleeding is unlikely in the next twenty-four to forty-eight hours, whereas if it is lower than 30%, much bleeding is almost inevitable. BIGGS finds that 1000 ml. of fresh *plasma* given intravenously in forty-five minutes usually raises the A.H.G. level of a severely affected patient to between 18% and 30% of normal. If a plasma-transfusion has been effective, the clotting-time of the blood will be normal, and this is a useful and rapid criterion. The effect unfortunately lasts only a few hours; in eleven hours the activity is halved, in twenty-four hours it has gone. It is therefore very difficult to maintain the desirable 30% level of A.H.G. for a long time, and if transfusions of 1000 ml. of plasma are given once daily the A.H.G. level will be below 30% for most of the time. Even this minimum represents transfusion of 2 pints of fresh donor blood daily, and that alone is difficult enough to secure; larger and more frequent transfusions are hardly ever practicable. For major operations a fuller correction of the antihæmophilic-globulin deficiency is essential, and here the use of animal A.H.G. has proved life-saving. In another paper Dr. MACFARLANE and his co-workers [4] record their experience with animal A.H.G. and human plasma in 13 patients who had to have surgical treatment.

The use of antihæmophilic globulin prepared from ox-blood was first reported by MACFARLANE and his colleagues in 1954.[5] BIDWELL [6] has since prepared antihæmophilic fractions from ox-blood and from pig-blood that can have activity up to 8000 times that of the same weight of fresh human plasma-protein. Unfortunately the use of these animal products is strictly limited by their antigenicity; this means in practice that they can be given for ten to fourteen days and then not again because of progressively severe allergic responses. And it is likely that once these animal products have been given intravenously to a patient, they can never be used again for that patient. It is for this reason that the use of animal antihæmophilic globulin should be restricted to covering absolutely necessary surgical procedures. By using A.H.G. from different animals it is possible to prolong the period during which the A.H.G. in the patient's blood can be kept at a satisfactory level, and MACFARLANE et al. describe patients who were treated in this way by bovine and then pig A.H.G. to secure healing of difficult wounds. The amount of A.H.G. given to these patients was equivalent to 2–4 litres of plasma daily—i.e., to blood from four to eight donors every day for one to three weeks. The human A.H.G. concentrate of KEKWICK and WOLF [2] is given in a dose of a tenth of the volume of plasma needed—i.e., 100 ml. of concentrate where 1 litre of fresh plasma is judged necessary from A.H.G. levels in the patient's blood. But the concentrate has to be worked up from fresh human blood, and it is still not certain whether it can be safely given in frequently repeated doses. All the present A.H.G. concentrates, human and animal, contain much fibrinogen—KEKWICK and WOLF's contains 70%—and probably small quantities of other proteins too. These may be antigenic from the start, or be rendered antigenic during processing. Consequently efforts are being made to prepare A.H.G. concentrates free from these contaminants in the hope that they will be less antigenic or even non-antigenic. Meanwhile it is worth reading with care the case-histories of the last 5 patients of MACFARLANE et al.[4] These patients were admitted for surgery but

1. *Lancet*, 1957, i, 677.
2. Kekwick, R. A., Wolf, P. *Ibid*, p. 647.
3. Biggs, R. *Ibid*, Aug. 17, 1957, p. 311.
4. Macfarlane, R. G., Mallam, P. C., Witts, L. J., Bidwell, E., Biggs, R., Fraenkel, G. J., Honey, G. E., Taylor, K. B. *Ibid*, Aug. 10, 1957, p. 251.
5. Macfarlane, R. G., Biggs, R., Bidwell, E. *Ibid*, 1954, i, 1316.
6. Bidwell, E. *Brit. J. Hæmatol.* 1955, **1**, 35, 386.

were successfully treated conservatively: in 2 acute appendicitis had been diagnosed, but each had in fact a retroperitoneal hæmatoma; 2 had gastro-intestinal hæmorrhage, probably started off by taking aspirin; the 5th turned out to have Christmas disease, and he had a retro-orbital hæmatoma. All these patients were satisfactorily treated by plasma and fresh-blood transfusion, without any operation.

Dental disease and dental extractions are among the commonest reasons for admission to hospital of hæmophilic patients. Mr. WISHART and his colleagues, on p. 363 of this issue, describe their experience at Oxford. They accept the view that animal A.H.G. should not be used for covering dental extractions; they accept the necessity for transfusing fresh plasma in large enough amounts just before the extractions, so plasma from 4 pints of fresh blood was used. This was combined with the use of proper dental splints made individually for each patient, following the example of MATHESON [7] and others. Such measures were largely successful and only a minority of patients needed more than the 4 pints of blood, but 1 needed 18 pints.

Another point dealt with is the toxicity and fate of injected animal antihæmophilic globulin. Dr. SHARP and Dr. BIDWELL (p. 359) have found that toxicity, apart from antigenicity, is not important. The fate of the injected A.H.G. should be discovered because the effects decline so swiftly. But despite the use of ingenious techniques, they were unable to solve this problem; A.H.G. is not absorbed in the cells of the reticulo-endothelial system as is γ-globulin, and does not appear to be excreted in the urine.

Hæmophilic bleeding can now be controlled in nearly every patient, the most dangerous form being inaccessible alimentary-tract bleeding. Minor operations, such as dental extraction, can be carried out in properly equipped departments. Such departments must clearly be in close liaison with a blood-transfusion centre so that supplies of fresh blood and plasma can be obtained on demand. If dental work is to be undertaken, the department must be able to coöperate with a dental member of the staff who will do this work regularly. The Medical Research Council's hæmophilia committee and the Ministry of Health are responsible for arrangements whereby in six hospitals in London, ten elsewhere in England, four in Scotland, and one in Belfast there are now departments which are prepared to investigate suspected cases of hæmophilia, treat their bleeding when necessary, and carry out at least dental operations. These departments are mostly, but not all, in teaching hospitals. This does mean that any doctor should be able to obtain help with these patients and has no need to struggle on unaided when bleeding does not stop within a few hours. At present the use of animal antihæmophilic globulin has to be limited to the few departments carrying out research work; we are still a long way from having A.H.G. concentrates that are suitable for general use. This means that, as hitherto, major surgery in a hæmophilic patient should be avoided unless there is no other means of treating him; and, even then, he should be sent to one of the specialised centres, such as the Postgraduate Medical School in London, the Radcliffe Infirmary in Oxford, or the Manchester Royal Infirmary, where adequate facilities are assured. In these days of air transport, as some of MACFARLANE's case-records show, this presents no difficulty.

7. Matheson, W. S. *Brit. dent. J.* 1949, **87**, 312.

Mental Defect, Tetraplegia, and Ichthyosis

A NEW syndrome—mental defect, tetraplegia, and ichthyosis—has been described in Sweden by SJÖGREN and LARSSON.[1] In 1955 they found 5 patients with this association of disorders in the institutions for mental defectives of Västerbotten, which is the second most northerly county of Sweden. They then searched the records and found 4 similar patients, of whom 1 was a cousin of a child in the first group. Among these 9 affected individuals, there were two pairs of sibs. An account of 2 of these patients and of a cousin of a 3rd has been published by SÖDERHJELM and ENELL.[2]

The mental defect was severe, usually at the level of idiocy. The ichthyosis was clinically and histologically similar to congenital ichthyosiform erythrodermia. The spasticity affected all four limbs, the legs more than the arms. Spastic diplegia and mental defect are commonly associated, autosomal and sex-linked, recessive forms being known though exceptional.[3,4] It is the third part of the triad—ichthyosis—which is unusual. SJÖGREN and LARSSON learned from Dr. LINSONNE, the chief surgeon of the main hospital in Stockholm for the treatment of spastic patients, that there were only 2 patients in the hospital records who, in addition to spasticity and mental defect, had ichthyosis. But three of the four parents of these 2 children came from the north-eastern coastal district of Västerbotten and had a common lineage with 1 or more of the Västerbotten patients.

Starting with the 9 patients from seven sibships as their index cases, SJÖGREN and LARSSON embarked on a genealogical investigation, of a kind which was possible only because of the excellent Swedish records and parish registers. In all, 28 affected individuals were found in these families, 3 of whom had the additional sign of macular retinal dystrophy. Analysis of the pedigrees showed that the criteria for recessive inheritance were fully satisfied. The majority of the couples who had had affected children were cousins (though none first cousins) and the proportion of affected brothers and sisters of the index cases was close to 1 in 4. Further, all but four of the twenty-four known parents of affected children could be traced back to a small group of individuals living in the coastal districts of the county in the 18th century. For example, five of the affected sibships could be traced back through six, seven, or eight generations to Olof T. and Gunilla J., who were born in 1705 and 1708. In three families the line is through one parent and in two families through both. Another two families were traced back in each, through both parents, to Abraham A., born in 1767, and Anna E., born in 1772.

SJÖGREN and LARSSON plausibly conclude that most of the recessive genes responsible for this syndrome originated in a single gene mutation, which was

1. Sjögren, T., Larsson, T. *Acta psychiat., Kbh.* 1957, **32**, suppl. 113.
2. Söderhjelm, L., Enell, H. *Nord. Med.* 1957, **57**.
3. Böök, J. A. *Acta Genet.* 1953, **4**, 345.
4. Blumel, J., Evans, E. B., Eggers, G. W. N. *J. Pediat.* 1957, **50**, 454.

already widespread in the eastern coastal seaboard of Västerbotten County in the early 18th century, and therefore happened as early as, or earlier than, the middle of the 14th century. They estimate that 1 in 80 of the population of the county now carries the gene. It is interesting that they found 2 affected children, not included in the series, in the mental institution of that section of the county of Jämtland which is just south of Västerbotten. These children were of Lapp race. There is a suggestion here (though SJÖGREN and LARSSON do not make the point and may have reasons against it) that the mutation may have been present in the native inhabitants before the Swedes themselves intensively colonised the county in the 14th century.

Annotations

POLLUTED COASTS

DURING an epidemic of poliomyelitis we have only ourselves to blame if the laity vent their ideas on the disease without much regard for our *amour-propre* or for the established facts of epidemiology. It is a frightening disease (though less so than the public thinks), we have spoken on the subject with uncertain and divided voices, and except for vaccination no method of control suggested by our profession has been proved of much value. This year we have been spared the wilder flights of popular fancy, and the much-publicised suggestion that bathing in water polluted by sewage plays a part in spreading infection [1] is a reasonable one.

We know that for every person who dies of poliomyelitis—300–800 each year in England and Wales—another 9 suffer from non-fatal infections with or without paralysis. This figure must be multiplied many times—a hundred-fold is a moderate guess—to give the number of persons without symptoms who excrete the virus for several weeks after infection. As might be expected the virus can be isolated from the sewage of any town where a few infections have occurred. Inland this probably does not matter much, but almost every seaside town empties its effluents into the sea with little or no treatment. It is a nasty habit begun with the best of intentions in the middle of the last century and perpetuated with little regard for the increase in the population, the new fashion of bathing, and advances in our knowledge of bacteriology. It has been calculated that each yard of the Lancashire coast receives forty large bucketfuls of raw sewage every day.[2] This is probably exceptional, but evidence that the ocean currents do not always carry sewage away from the shore may be seen in many places. The virus of poliomyelitis has not been found in these waters—the technical difficulties are considerable—but typhoid bacilli have been found quite often in sea-water from resorts in England and elsewhere. The virus has been isolated from polluted river water, and an association between bathing in rivers and infection has been suspected for many years. The greatest incidence of the disease coincides with the peak of the bathing season.

It is a sensible thesis but not entirely convincing. Those most likely to acquire infection are those in the closest physical contact with the source of infection. It is a disease of crowds and, whether they bathe or not, those who flock to seaside resorts are a part of an intimately jumbled crowd. Coming from diverse parts of the country they have the opportunity of spreading infections more widely, and this alone might increase the likelihood of poliomyelitis in any holiday resort. The proportion of children in the seaside crowd is high, and there is some evidence that children are not only more susceptible to infection but also a more potent source of infection than adults. The connection, if any, between bathing and poliomyelitis may be indirect. The part that fatigue plays as an adjuvant to infection is still uncertain, but children are likely to be over-tired on holiday and especially by swimming. Lastly, in this or in any other epidemic year, there are no figures to suggest that the incidence of the disease is higher in the seaside resorts than elsewhere.

No-one would care to say that poliomyelitis cannot be acquired by bathing in polluted water, salt or fresh. The question is whether at the time of an epidemic this habit carries an especial risk or one greater than living in a crowd containing many children. We have not the evidence to answer this even tentatively, but it is probably significant that very few, if any, enteric infections can be ascribed to bathing in waters known to contain typhoid bacilli. In both diseases infection occurs by the mouth: few of us can swim without taking a little water aboard, but the amount is so small that we shall be very unlucky if we receive an infectious dose of anything. Life for most of us would be hard to bear if we felt compelled to avoid every activity which laid us open to a minimal chance of acquiring any illness. "Those who wish to die in bed had better stay in bed." A distinguished sanitary engineer has said that he would not let his children bathe at a typical seaside resort. Perhaps he is right, but the journey to and from the coast by car is probably a more hazardous undertaking.

1. *Times*, Aug. 13 and 14, 1957.
2. Report, Lune and Wyre Fishery Board, 1945.

B.C.G. VACCINE

A YEAR ago Lorber et al.[1] reported a trial of a British freeze-dried B.C.G. vaccine. In a second report [2] they compare its sensitising properties in infants with those of the Danish liquid vaccine now used in this country. A batch of freeze-dried vaccine, with a viable-cell count of about 10×10^6 per ml., gave as high a tuberculin conversion-rate as the liquid vaccine—virtually 100%. The vaccination lesions had almost the same mean diameter, and there was a slightly smaller incidence of significant enlargement of axillary nodes. There can now be little doubt that this vaccine is as good a sensitising agent as the imported liquid vaccine; and, being freeze-dried, it has obvious practical advantages. The vaccine has been produced through the foresight and pertinacity of a large pharmaceutical firm, which began work on it at a time when B.C.G. vaccination was officially neglected in this country. Their product is still not available in Great Britain through the Ministry of Health.

The Medical Advisory Committee of Research Foundation in the United States has now issued a report [3] on B.C.G., in which they point to the need for vaccination in that country because of the persistently high number of new cases—in 1954 about 100,000, which was more or less the same total as in 1930. They endorse the American Trudeau Society's recommendation that B.C.G. should be used for the vaccination of infants and children in areas of high prevalence and for those who may be unavoidably exposed to infectious patients. These recommendations have already been adopted by the United States Public Health Service. The committee also recommended that B.C.G. should be made available to any licensed physician. The United States has been even slower than this country in using this valuable method of saving life; but those who control the preventive measures in Great Britain might well take note of the respect shown by the American committee for the freedom of each individual doctor.

1. Lorber, J., Hart, C. B. S., Farmer, P., Muggleton, P. W. *Tubercle, Lond.* 1956, **37**, 187.
2. Lorber, J., Farmer, P., Muggleton, P. W., Hart, C. B. S., Menneer, P. C., *Ibid*, 1957, **38**, 227.
3. Report by the Medical Advisory Committee of Research Foundation. *J. Amer. med. Ass.* 1957, **164**, 951.

AN ORAL DIURETIC

MOST doctors would agree that the development of an effective diuretic agent suitable for administration by mouth is one of the most urgent necessities in general practice. The organic mercurial agents substantially reduce œdema due to congestive cardiac failure only when they are given by deep intrasmuscular injection, which is disliked by both patient and doctor. The study of various 6-aminouracils[1–6] eventually led to the introduction of aminometradine (' Mictine ') and several reports on its therapeutic use have appeared.[7–9] It is a synthetic non-mercurial compound containing a pyrimidine ring. Chemically it is 1-allyl, 3-ethyl, 6-aminotetrahydropyrimidinedione. Alkyl substitution on both the 1- and 3-positions appears necessary for a diuretic effect, but little is known connecting the chemical structure with the action on the kidney.

The drug is effective when given by mouth, but its metabolism has not yet been elucidated. A constant dose does not achieve its full effect until a few days have elapsed—suggesting that excretion or destruction of the drug may be relatively slow resulting in accumulation in the body.[10] The chief toxic features are nausea, anorexia, and vomiting; and these may be extremely troublesome, preventing the administration of fully effective doses. In a recent trial, the drug (given in the relatively moderate daily dose of 600 mg.) had to be discontinued in a third of the patients on account of these side-effects.[9] Toxic reactions usually appear early in the course of treatment, and if the first week passes without them they are unlikely to develop later unless the dose is increased.

Aminometradine does not alter the glomerular filtration-rate or renal plasma-flow in dogs, and is presumed to act by inhibiting the reabsorption of sodium and chloride in the renal tubules. In this way it resembles the organic mercurial diuretics, but there are certain differences. The excretion of potassium and chloride is less with aminometradine; and sodium and chloride are excreted in about equimolecular proportions in contrast to the rather higher proportion of chloride commonly seen after an injection of mersalyl. The precise mode of action of aminometradine on the renal tubule is unknown, but neither succinic dehydrogenase nor carbonic anhydrase is inhibited.

Aminometradine is put up in 200 mg. tablets, and two or three a day are commonly prescribed in the treatment of mild congestive cardiac failure. Larger amounts usually cause toxic effects. Diuresis may not begin until the second or third day after starting treatment. The drug should be given in short courses of two or three days, with a day's rest in between, to reduce the liability to toxic effects induced by accumulation in the body.

Assay of the effectiveness of diuretic agents is difficult for so often diuresis follows rest in bed quite apart from the administration of any drugs.[8] Nevertheless, clinical trials of aminometradine have shown that it increases the excretion of electrolytes and water in congestive cardiac failure and hepatic cirrhosis.[11 12] There is general agreement that it is not so potent as mersalyl, but in comparing them allowance should be made for the slow response to aminometradine and the brisk one to mersalyl. In the first twenty-four hours after an injection of mersalyl there is a large output of urine, often followed by a diminution below normal on the succeeding day; thus, over a period of a week there may not be a great difference in the total response between two injections of mersalyl and two two- to three-day courses of aminometradine. In the treatment of moderate or severe congestive cardiac failure, mersalyl is undoubtedly the diuretic of choice, for rapid relief of the œdema is required; but after an initial period of parenteral treatment, the patient may sometimes be relieved of the discomfort of repeated injections by substituting aminometradine by mouth, and long-continued therapy may ward off recurrence of œdema. The drug may also be useful occasionally in the initial treatment of mild œdema in the ambulant cardiac patient.

The action of aminometradine may be potentiated by combination with other diuretic agents. Chloride excretion is increased by both aminometradine and mersalyl, and the administration of ammonium chloride may aid their action by preventing undue depression of the plasma-chloride level. Acetazolamide (' Diamox ') increases bicarbonate excretion; the plasma-bicarbonate then falls and the chloride rises—the reverse of the action of the other two drugs. There is thus a good basis for giving alternating courses, of a few days' duration, of aminometradine and acetazolamide. Hanley[10] has suggested schedules of treatment combining these agents, and draws attention to the importance of not giving ammonium chloride in addition to the combination of acetazolamide and aminometradine as this may lead to a dangerous metabolic acidosis.

A safe and effective oral diuretic will find great use in therapeutics. Many promising compounds are now being investigated, but so far none is comparable in effect with intramuscular mersalyl. Aminometradine itself is clearly useful, particularly in preventing œdema in the cardiac patient on the verge of congestive failure; but in the more severe case we still have to rely on the older and more powerful, though less convenient, agents.

NECROSING POLYARTERITIS IN RHEUMATOID ARTHRITIS

IN the past five years there have been several published accounts of vascular lesions, resembling those of polyarteritis nodosa, in patients with rheumatoid arthritis.[13–18] Treatment with cortisone was early suspected of being concerned in this complication, and later experience has increased this suspicion. Arteritis is, of course, a recognised feature of the morbid histology of rheumatoid arthritis, but in the absence of treatment with steroids this has generally taken the form of subacute cellular infiltration in and around vessel walls, with necrosis.[19] A less common vascular complication—and again one in which steroids are probably not implicated—is obliterative endarteritis. Bywaters[20] has drawn attention to this complication, in which the lesions vary from small infarcts—presenting as brown lesions of the nail-fold, nail-edge, or digital pulp—to gangrene of all four limbs and visceral lesions. Histologically the vascular lesions resemble somewhat those seen in scleroderma and, more closely, those of systemic lupus erythematosus.

1. Papesch, V., Schroeder, E. F. *J. org. Chem.* 1951, **16**, 1879.
2. Kattus, A. A., Newman, E. V., Franklin, J. *Bull. Johns Hopk. Hosp.* 1951, **89**, 1.
3. Kattus, A. A., Arrington, T. M., Newman, E. V. *Amer. J. Med.* 1952, **12**, 319.
4. Greiner, T., Gold, H. *J. Amer. med. Ass.* 1953, **152**, 1130.
5. Hellman, E., Altchek, R., Enselberg, C. D. *Amer. Heart J.* 1952, **44**, 615.
6. Spencer, A. G., Lloyd-Thomas, H. G. *Brit. med. J.* 1953, i, 957.
7. Platts, M. M., Hanley, T. *Ibid*, 1956, i, 1078.
8. Caccamo, L. P., Pringle, B. H., Hissong, D. E. *Amer. J. med. Sci.* 1956, **232**, 289.
9. Wener, J., Knight, A. *Canad. med. Ass. J.* 1957, **76**, 952.
10. Hanley, T. *Practitioner*, 1956, **177**, 744.
11. Tatge, W. A., Winnik, D. E., Spencer, G. N. *Amer. J. med. Sci.* 1956, **232**, 175.
12. Nissen, N. I., Zachau-Christiansen, B. *Acta med. scand.* 1956, **154**, 349.
13. Etheridge, E. M., Hoch-Ligeti, C. *Amer. J. Path.* 1952, **28**, 315.
14. Levin, M. H., Rivo, J. B., Scott, W., Figueroa, W. G., Fred, L., Barrett, T. F. *Amer. J. Med.* 1953, **14**, 265.
15. Robinson W. D., French, A. J., Duff, I. F. *Ann. rheum. Dis.* 1953, **12**, 323.
16. Weinberger, H. J. *Ibid*, p. 324.
17. West, H. F., Newns, G. R. *Lancet*, 1953, ii, 1123.
18. Finck, P. A. *Arch. Path.* 1955, **60**, 374.
19. Cruickshank, B. *Ann. rheum. Dis.* 1954, **13**, 136.
20. Bywaters, E. G. L. *Ibid*, 1957, **16**, 84.

Some statistics about the rôle of cortisone in the genesis of the necrosing type of polyarteritis have come from the Mayo Clinic.[21] The incidence of vascular lesions of various types was ascertained in 52 cases of rheumatoid arthritis which came to necropsy. 38 patients had received no cortisone, and vascular lesions were found in 8 of these. In 5 the lesions were confined to the heart, and were judged to be related to rheumatic fever; the other 3 had more active acute vasculitis limited to one organ or to a single vessel. Lesions similar to those of classic polyarteritis nodosa were confined to patients who had been given cortisone, and were found in 4 of the 14 cases in this group. At the International Congress on Rheumatic Diseases in Toronto this summer, J. J. Bunim reported that polyarteritis nodosa developed in 4 out of 49 cases of rheumatoid arthritis treated with prednisone; in 3 the complication declared itself while the dose was being reduced.

Slocumb et al.[22] have described polyarteritis nodosa as an occasional accompaniment of a syndrome which they regard as a "special" effect of long-continued hypercortisonism in patients with rheumatoid arthritis. (In this context "hypercortisonism" implies the effects of large doses of cortisone or of any steroid with similar activity, as well as of vigorous adrenal stimulation with corticotrophin.) This "special" effect develops as a rule after the well-known "general" effects of hypercortisonism ("moon-face," &c.) have been evident for several weeks or months. The characteristic features are cyclic swings of mood and of other symptoms. Increased fatigability, aching of muscles and joints, and emotional instability alternate with periods of stimulation associated with restless "drive" and relatively little aching. Care has to be taken not to mistake these developments, which are often accompanied by a rise in the erythrocyte-sedimentation rate, for a flare-up of arthritis. To these "special" features of hypercortisonism are added, on occasion, more sinister developments. These may simulate either systemic lupus erythematosus or polyarteritis nodosa. The argument that patients with these complications were, in fact, hitherto unrecognised cases of systemic lupus erythematosus or polyarteritis nodosa is to some extent countered by the varying incidence of the lupus-erythematosus-cell phenomenon in cases observed by Slocumb and his colleagues. Among patients with rheumatoid arthritis treated with cortisone, but with no signs of overdosage, the phenomenon was found in the same proportion of cases as in a group not treated with steroids—namely, in 5%. In cases with hypercortisonism the figure was 14%.

Here, then, is an apparent paradox, interesting in its implications and not yet resolved. The suppressive action of cortisone on the lesions of polyarteritis nodosa or of systemic lupus erythematosus is undeniable; yet in certain circumstances the same agent seems to precipitate some of the manifestations of either disease. Can this be a simple matter of cortisone "poisoning," or a more subtle upset of hormone-tissue relationships? Slocumb et al. hold that reactivation of arthritis does not accompany the development of arteritis or the manifestations of systemic lupus erythematosus; nevertheless other observers, including Bunim, have felt that these developments often occur when the dose of cortisone is being reduced, or when the effect of an unaltered intake is slowly dwindling. Treatment of the "special" effects of hypercortisonism is, in the view of the Mayo Clinic group, a matter of very slow reduction in dosage of steroid; but it is clear from their account that the clinician has to lead his patient out of this unpleasant situation by a hard and precarious path. It would be useful to know whether severe and intractable cases of rheumatoid arthritis are peculiarly liable to this complication of treatment with steroids. Certainly they have not been encountered in therapeutic trials of cortisone in cases selected for their comparatively short duration rather than for severity. The most useful warning of the development of polyarteritis nodosa in many of the cases described has been the onset of peripheral neuritis.

21. Kemper, J. W., Baggenstoss, A. H., Slocumb, C. H. *Ann. intern. Med.* 1957, **46**, 831.
22. Slocumb, C. H., Polley, H. F., Ward, L. E. *Proc. Mayo Clin.* 1957, **32**, 227.

BRONCHIAL ADENOMA

BRONCHIAL adenoma is the commonest simple lung tumour, and unlike bronchial carcinoma is commoner in women than in men. It is occasionally grey, white, or yellow, but usually it is red because of a vascularity which may give rise to brisk hæmorrhage spontaneously, or at biopsy. Most adenomas are situated in the larger bronchi, and, apart from hæmoptysis, symptoms and signs are due to bronchial blockage[1]—at first perhaps unilateral wheezing and obstructive emphysema, and later atelectasis, suppuration, and productive cough. The minority of tumours that originate in small, peripheral bronchi, or those that are largely exobronchial, may be silent,[2] and diagnosis may follow investigation of a "coin" shadow seen in a routine chest film. An adenoma almost invariably arises from a single site in the bronchial tree, but Felton et al.[3] have recorded 2 examples of multicentric lesions, and Overholt et al.[4] 4 more.

Although bronchial adenomas are classed as simple tumours, metastasis is well known.[5–12] Nevertheless, the malignant potential observed in Overholt's study is probably greater than would have generally been expected. Metastasis was seen in 9 (15%) of 60 cases—in 6 to associated lymph-glands and in 3 to distant organs. Moreover, 2 of the 6 patients with lymph-gland metastases subsequently died as the result of generalised metastases. There was no relationship between duration of symptoms and curability. A long history neither jeopardised nor guaranteed the success of surgical resection: patients with histories of up to 45 years' duration were apparently cured, but on the other hand 2 patients with histories of six and seven years died from generalised metastases two and four years respectively after operation.

Two main histological varieties of bronchial adenoma are usually described[10]—a carcinoid type and a less common cylindromatous type which is more invasive than the other and which, because of its predilection for a central site near the carina or in the trachea, may produce death by suffocation. There were only 2 cylindromas in Overholt's series and neither gave rise to metastases.

Bronchoscopic resection is, of course, no longer done—the tumour and associated lymph-glands are excised at open operation. Secondarily infected lung tissue usually also has to be removed, but if the lung has escaped serious injury it may be possible to resect only that part of the bronchus in which the tumour is situated and reconstruct the airway.[4 11]

1. Foster-Carter, A. F. *Quart. J. Med.* 1941, **10**, 139.
2. Good, C. A., Harrington, S. W. *Proc. Mayo Clin.* 1953, **28**, 577.
3. Felton, W. L. II, Liebow, A. A., Lindskog, G. E. *Cancer*, 1953, **6**, 555.
4. Overholt, R. H., Bougas, J. A., Morse, D. P. *Amer. Rev. Tuberc.* 1957, **75**, 865.
5. Mallory, T. B. *New Engl. J. Med.* 1938, **218**, 391.
6. Adams, W. E., Steiner, P. E., Bloch, R. C. *Surgery*, 1942, **11**, 503.
7. Anderson, W. M. *J. thorac. Surg.* 1943, **12**, 351.
8. Laff, H. I., Neubuerger, K. T. *Arch. Otolaryng., Chicago*, 1944, **40**, 487.
9. Van Hazel, W., Holinger, P. H., Jensil, R. J. *Dis. Chest*, 1949, **16**, 146.
10. Liebow, A. A. Tumours of the Lower Respiratory Tract. Atlas of Tumour Pathology. Section v. Fasc. 17. Armed Forces Institute of Pathology, Washington, 1952.
11. Thomas, C. P. *Lancet*, 1954, **i**, 1.
12. Kincaid-Smith, P., Brossy, J. J. *Thorax*, 1956, **11**, 36.

Public Health

TUBERCULOSIS CASE-FINDING IN THE AGED

O. D. BERESFORD
M.D. Wales, M.R.C.P.
CHEST PHYSICIAN, POOLE CHEST CLINIC

THE search for pulmonary tuberculosis in the aged has had little attention in the past, and if the disease is to be brought finally under control more strenuous efforts must be made to deal with this important reservoir of infection.

During a survey of tuberculin skin sensitivity in the elderly, in which those that were tested had chest radiographs, it was decided to extend the scope of the investigation by radiographing as many old people as possible. As the tuberculin testing had provided access to the various geriatric units and old folk's homes, it was thought that enough people would be radiographed to indicate the amount of tuberculosis in this age-group.

There were many difficulties. One large group was in an isolated geriatric unit with no X-ray apparatus, and it proved impracticable to radiograph any of these. In the geriatric units with X-ray apparatus, a high proportion of those tuberculin-tested were radiographed, and it was easy to persuade patients to accept this; but many of the bedridden could not be examined in this way.

The healthy people in old people's homes were invited to attend for radiography irrespective of whether they had been tuberculin-tested. To ensure maximum attendance, transport was supplied to take them to the X-ray unit and back. The homes were visited and a little talk given to the old folk explaining what it was all about and urging them to take advantage of the offer.

Lastly, special sessions of the mass-radiography unit were held for the aged, and propaganda was distributed through the various Darby and Joan clubs and voluntary organisations concerned with the welfare of old people. A leaflet with details of the scheme was given to old-age pensioners as they collected their pension at the post office. The usual press notices of the survey were also distributed.

RESULTS

Old people radiographed on days other than those specially arranged for them are not included in this work. The results in the others are shown in the table.

—	In hospital	In old folk's homes	General populace
No. of old people ..	..	659	26,000
No. tuberculin-tested ..	..	395	..
No. radiographed ..	193	230	394
No. needing surveillance	12	20	17
No. of active cases ..	1	1	1

DISCUSSION

The number of cases of bacteriologically proved active tuberculosis discovered in this survey seems small, but the real value lies in the discovery of the presumed tuberculous lesions which need surveillance and enable adequate contact examination to be carried out. The difficulties in obtaining chest radiographs of the elderly out of hospital were enormous and seem insurmountable. Their main objection to being radiographed seemed to be that "it didn't matter as they were so old." Possibly behind this was the fear of what would happen to them if a lesion was discovered. Another reason for not attending was the presence of some disease which precluded travelling: the most common excuse in this connection was a "bad heart." Some people objected on principle to being radiographed and others regarded it as some form of devilment.

In spite of much propaganda, less than 2% of the aged general populace volunteered for radiography. Even in the old people's homes, where strenuous efforts were made to obtain a maximum response and transport was supplied, less than 40% attended.

It seems that for a number of reasons old people will not be radiographed, and, since there is a substantial amount of tuberculosis in this age-group, ways and means must be found of getting this examination made. Heaf [1] has suggested that chest radiography should be a condition for payment of an old-age pension. This might prove difficult and cause hardship, but it should be relatively easy to ensure that people entering old folk's homes are radiographed before admission.

For the remainder of the ever-increasing aged population, it seems that any measures short of compulsion will meet with little response in obtaining chest X-rays.

I wish to thank Mr. S. H. Hunter, head postmaster of Bournemouth, and Miss B. Evered, of the Bournemouth Women's Voluntary Services, for their help in distributing to the elderly people information about the project. Special sessions of the mass-radiography unit were arranged in coöperation with Dr. J. Stuart Robertson, the medical director.

The expenses of the work were defrayed by a grant from the research committee of the South West Metropolitan Regional Hospital Board.

Poliomyelitis

Uncorrected notifications of poliomyelitis in England and Wales in the week ending Aug. 10 were (previous week's figures in parentheses): paralytic 183 (141), non-paralytic 145 (119), total 328 (260). 2694 cases had been recorded up to the 32nd week of 1957—the highest total since 1950, when the corresponding figure was 2983.

The Ministry of Health's special team on poliomyelitis vaccine left for Canada and the United States by air last Saturday. Its members are Dr. G. A. Clark, deputy chief medical officer of the Ministry, and Dr. W. L. M. Perry, director of the Medical Research Council's department of biological standards. Their task is to explore the possibility of manufacturing British poliomyelitis vaccine abroad.

New York City has had a week free of poliomyelitis for the first time since records began in 1916. From Aug. 7 to 14 not a single case was reported. Last year there were 10 cases in the period Aug. 7–16, and the average for that period over the past ten years has been 73 cases. 70% of persons under the age of 20 in the city have had at least one dose of vaccine.

Influenza

With outbreaks reported from South America, Asian influenza has now appeared in every continent. The disease, which remains mild, is increasing in the United States and many parts of Africa, but in general it is becoming less prevalent elsewhere. In this country the disease is suspected, but not yet confirmed, in a boys' naval training-school in Hampshire, among American airmen in the home counties, members of the Sheffield Wednesday Football Club, and sailors in Belfast.

In the Hampshire outbreak,[2] 36 boys were taken ill while attending a Y.M.C.A. training-school at Botley. 14 were taken to hospital in Poole to ease the strain on accommodation at Botley. Asian influenza was suspected because of the speed with which the infection spread. The boys, who were attending a Merchant Navy training course, are between 15 and 17 and come from all parts of the country. The illnesses have been mild and all those affected are said to be progressing favourably.

In the United States, influenza vaccine is being produced by several firms, and the first 500,000 doses have been released. It is expected that 60,000,000 doses will be produced by Feb. 1, half of it for the armed forces, and that the vaccine will protect 70% of those vaccinated.

1. Heaf, F. R. G. *Brit. med. J.* 1956, ii, 1383.
2. *Times*, Aug. 19.

In England Now

A Running Commentary by Peripatetic Correspondents

"JUST another pneumonia, sir." Such was my introduction to William, a burly self-conscious lad of 12, lying rather awkwardly in bed, for he had reached an age when rapidly growing limbs seemed at strange variance with a mind still that of a child. But why should a strapping lad have pneumonia at the height of summer? No-one could tell me, but something about his face made me pause and it was an unfilled line on his temperature chart which led us to his story.

He was seven years old when his mother died. For the next five years he was buffeted from relative to relative and house to house, some good, some bad, some kind, some harsh. Each move, bringing fresh problems, left its mark; but he learnt to imprison his unhappiness, and herein lay the root of the gradual atony which paralysed his colon, causing it to spill its contents like a brim-filled bowl.

After five years an indifferent succession of housekeepers came to an end. At last William came home—to a new home and to a new mother. When she welcomed him she did so wishing to love him as her own son. But on finding his soiled clothes in her laundry bag for the first time, she promptly remonstrated with her husband: "look what *your* son has given me to wash!" "We'll soon see about that," he said, and a few seconds later the hoarse cries of a broken-voiced adolescent tore through the house.

Uneasy peace reigned after this episode—uneasy because William sought to conceal his physical weakness by all possible means, for he alone knew that it lay beyond his control. He accumulated vast hoards of old rags and newspaper to insinuate between clothes and skin. One night, after he had gone to bed, his father demanded the previous day's paper, and in a search from room to room they chanced upon his hoard—some used, waiting to be destroyed. "There's only one way to cure him of this for once and for all," said his father, making for the stairs. The bruises on his face, which had first arrested my attention, covered his body.

Doctors often scoff at the notion that pneumonia springs from cold and damp. The fact remains that this boy, forced to abandon his first defence, for five days washed his clothes in the river on his way home from school, donning the sogging garments each day before returning home. On the sixth day his breathing came in short sharp gasps and he spat rusty sputum into his handkerchief. A doctor was summoned.

* * *

In my young days when you had to treat a stomach ulcer the only argument was about various operative procedures bearing unpronounceable Continental names: but not now. Same with asthma: ephedrine and desensitisation, all very well in their way, are giving way to psychotherapy. Everything from flat feet to falling hair is plunged into the psychosomatic melting-pot and soon we shall have to do the Rorschach test and Minnesota multiphasic personality inventory on every new admission, just like some people used to take the blood-pressure. The old simple doctrine of locating the diseased organ and happily hacking it out is giving way, viscus by viscus, to the inevitable onslaught of statistical method, psychological research, and, of course, drugs. True, some surgeons are fighting a skilful rear-guard action and others pretend to be allies, but these leucotomies and hypophysectomies won't last. Even a broken leg can be attributed to psychological "accident proneness."

As a healthy hearty houseman these things didn't worry me much: I regarded the trend with a benign eye and it did, after all, give you the excuse to send some of your more tiresome cases round to the trick-cyclist. But with middle-age creeping on, and the old pipes and joints beginning to bend and creak, the matter takes on an urgent personal aspect. Why, even when you go to one of your old friends with a good clean healthy organic lesion like a gardener's slipped disc, the first thing he does is to talk about emotional tension and neuromuscular imbalance, and ask you if you're happy with your wife!

* * *

My week's "holiday" was just ending when I received an invitation to submit exhibit(s) to the Doctors' Hobbies Exhibition. The first heading was "painting" which seemed singularly apt. But how to transfer my front door to London; let alone the "smallest room" and the wash-house. Perhaps it would be permissible to send photographs of one's work, but there would be a danger of these being diverted into the photographic section, and it would be difficult to infuse any artistic merit into *A Study of White Enamel from the W.C.*!

No, perhaps it would be better to turn to authorship, and write a monograph on *Philosophy for Senior Registrars, Based on an Analysis of Wilkins Micawber*—with an appendix on holidays at home, and occupationally therapeutic hints for the home decorator, gardener, electrician, motor mechanic, and general odd-job man.

* * *

Once upon a time there lived a poor young Doctor who developed appendicitis. But poor as he was, in his eagerness to be of Some Use—and remembering that two heads are better than one—he gave permission for the operation to be telecast over the hospital's private circuit for the instruction of guest-surgeons and fellow-students, who could be relied upon to call the operating surgeon's attention to unwarranted pilfering of organs and to pieces of equipment in danger of being Left Within.

Just as he was giving his name, address, and what-not to Nurse, and asking her when was her day off, a Wicked Fairy introduced some sunspots into the television circuit, and he appeared on channels 3–7 inclusive, except for North Hessary Tor which was on low-power pending completion. Before he was off the table, he was off the Register.

However, the poor young Doctor's Good Fairy saw to it that he married the Nurse, who became a leading star on I.T.V. and well able to support him in the style to which he rapidly became accustomed, and they lived happily ever after.

* * *

We have just returned, full of sadness as usual, from our annual fortnight's holiday in a remote corner of Wales. It appears, however, that our children do not share our sentiments. "Only thirteen more days and we shall be home again," announced our elder daughter at breakfast on the first day, and each morning began with a similar remark. Our younger daughter could not be enticed within yards of the water, and complained bitterly of the dogs on the beach and the spiders in the bungalow. On the last morning my wife said that it was a pity we couldn't spend three weeks there instead of two. To which our son, in his most lugubrious prep. school manner, replied: "Three weeks! It's bad enough having to waste two weeks of my holiday." My wife and I are already planning, with the children's approval, a long summer cruise for next year, while they enjoy a restful holiday at home.

* * *

After some months in general practice, I tried to analyse the way my prescriptions had varied with my feelings towards the patient. An interesting result: patients I don't like very much tend to get Mist. Gent. Alk., others that I hate have Mist. Pot. Brom. et Valerian, and ones that I positively loathe (happily few) are given Mist. Pot. Brom. et Assafetida, which their families make them keep in the shed at the end of the garden, dispatching them down there t.d.s., a.c.

* * *

It was a hot afternoon and the laparotomy had taken up most of it. The house-surgeon was dozing on a retractor and even the staff nurse had allowed her mind to wander as she automatically maintained a supply of swabs for the surgeon, who was endlessly mopping possible bleeding areas. At last he decided to close the peritoneum. "Swabs all right, nurse?" "Yes, I've got plenty thanks, sir."

* * *

Alas for you! Alas for me!
They've made a new discovery,
T'will make it harder still to die.
I wonder why? I wonder why?

Letters to the Editor

THE TEACHING HOSPITALS

SIR,—Your editorial of Aug. 10 gave a confused and gloomy impression of administrative procedure and capital development in the teaching hospitals. It also showed a disturbing ignorance of the more important facts.

Tenders for the erection of the first instalment of the new Guy's Hospital are now received. These are below the estimated cost and it is expected that their acceptance will be finally approved by the Ministry of Health in the next few days. Work will commence immediately after.

Plans provide for 378 surgical beds, new casualty and radiotherapy departments, a university departmental floor, and ten operating-theatres. The planning of the present scheme was not started until early in 1955, although it is true that it has drawn a great deal from an earlier scheme which had to be abandoned. All sections of the hospital have worked smoothly and swiftly together in its preparation, the Board and its planning committee and the medical committee. Great help has been received from the Ministry of Health and the local authorities.

If at least one of the twelve London undergraduate teaching hospitals is commencing the first instalment of a major rebuilding scheme (cost in excess of £2,000,000), the picture is nowhere near as bad as was painted in your editorial and probably reference to the Ministry of Health would produce evidence of other substantial expenditure on teaching hospitals.

To use "free money" to any great extent would curtail expenditure on medical research; it would be a policy of living for today at the expense of posterity; far better that it should be used carefully in conjunction with exchequer funds as in the case of Guy's and St. Thomas's Hospitals among others.

Guy's Hospital,
London, S.E.1.

B. LEES READ
Clerk to the Governors.

TREATMENT OF HIRSCHSPRUNG'S DISEASE

SIR,—May I comment on the letters of Mr. Cooling (Aug. 3) and Mr. O'Donnell (July 20)?

I did not discuss the question of impotence after operation because the Great Ormond Street cases are not yet old enough to allow the matter to be assessed adequately.

Mr. O'Donnell's statement that there is increased danger to the pelvic nerves during a revision operation, and mine that there is no ready plane of cleavage at the original dissection, are not contradictory. At the first operation the rectal wall can be easily identified, and, with care, dissection can be made on it; but during secondary operations recognition is more difficult. Then there is greater danger both of stripping the muscular layer and even entering the bowel, and of dissecting at a distance from the rectal wall.

Undoubtedly, Mr. Cooling is right in saying that children's hospitals get the severe early cases and rectal hospitals the patients who survive to adult life. But the numbers simply cannot be compared. The great majority need treatment early in life; without it, very few survive to adult life.

Like Mr. Cooling, I also look forward to reading a follow-up note of cases treated by State's method. I have done so for some time.

North Adelaide,
South Australia.

G. G. WYLLIE.

ECLAMPSIA

SIR,—May I, belatedly, enlarge on my explanation of the cause of eclampsia?[1] I suggested that pregnant women react to transplacental hormones from a fœtus; that the placenta is damaged by this reaction, endangering the life of the fœtus; and that "toxin" from the damaged placenta causes toxæmia and eclampsia.

Criticisms[2] of this hypothesis were not difficult to answer,[3] except that the fœtal and maternal hormones are identical, which makes it hard to understand why the mother should react. I now realise that it is not the fœtal hormones per se to which the mother reacts, but their anabolic effects. Rapid growth, the hallmark of anabolism, occurs earlier, like eclampsia, with a hydatidiform mole than with a fœtus.

In any growing fœtus anabolism must exceed katabolism; the faster the growth, the greater the excess of anabolism. But before pregnancy the mother's anabolism and katabolism are evenly balanced; when fœtal anabolic hormones (growth hormone, thyroxine, insulin, and androgen)[4] begin to pass into her and upset the balance, her katabolism is increased to compensate. Since œstrogenic steroids are mildly anti-anabolic,[5] the anabolic effect of androgens from a fœtus, though weak, should be more evident with a male child than a female one. The mother's response to the anabolic stimulus is to produce more hydrocortisone, which is the main katabolic hormone, in quantities which steadily increase as the baby and its anabolic influence grow. Increased secretion of corticoids in the middle of pregnancy has been reported.[6]

Physiological increases in hydrocortisone secretion lead to striæ (which, like toxæmia, are commonest in the first pregnancy), to sodium and water retention, and to an accelerated gain in weight. Excessive or pathological increases, as in response to abnormally strong anabolic stimulation, lead to œdema and mild hypertension, particularly when there is an excessive calorie intake, or the double hormone production of twins, or a large and rapidly growing baby (e.g., of a diabetic mother). Hydrocortisone production counterbalances the fœtal anabolic influence, and is more pronounced in young than in older mothers, more violent in the unacclimatised primiparæ than in previously sensitised multiparæ, and more in obese mothers (already straining to counteract anabolic tendencies) than in thin ones.

The most important contributory factor is carbohydrate intake. Growth hormone[4 5] and avitaminosis-B both interfere with oxidation of carbohydrates. The struggle between maternal hydrocortisone and the fœtal growth hormone becomes extra severe if the mother is consuming much carbohydrate. Most cases of toxæmia and eclampsia occur among excessive carbohydrate consumers, and beriberi renders a mother highly susceptible. Food shortage prevents excessive ingestion of carbohydrate. In war, famine, and certain tribes (e.g., wholly flesh-eating pigmies) toxæmia and eclampsia are either rare or non-existent.

I am convinced that there is an important link between the hydrocortisone-produced rise of blood-pressure in toxæmia and the onset of albuminuria—i.e., damage to the placenta. Vasospasm accompanies the rise in diastolic pressure, reducing blood and oxygen supply to the delicate villi of the placenta; and hydrocortisone, through its ability to break down protein into carbohydrate, damages the delicate, devitalised syncitium and villi. Debris or "toxin" is carried from the damaged (infarcted) area of placenta to the kidneys, leading to albuminuria and a much accentuated rise in blood-pressure.[7] In uncomplicated toxæmia, albuminuria is a post-embolic phenomenon and indicates great danger to mother and baby; infarcts are certainly present in the placenta. With hypertension but no albuminuria, there are often no infarcts—placental damage has been imminent but has not yet taken place.

1. Salzmann, K. D. *Lancet*, 1955, ii, 953.
2. Schuurmans, R. *Ibid*, p. 1294; *Ibid*, 1956, i, 161.
3. Salzmann, K. D. *Ibid*, pp. 48, 288.
4. Hubble, D. *Brit. med. J.* 1957, i, 601.
5. Gaunt, R. Dynamics of Growth Processes. Princeton, N.J., 1954; p. 183.
6. Venning, E. H. *J. Endocrin.* 1946, **39**, 253.
7. Young, J. *Proc. R. Soc. Med.* 1914, **7**, 307.

Death of the fœtus removes the anabolic stress, but leaves the damaged placenta. The contractions of labour may disseminate debris from this, precipitating eclampsia.

We are taught that women in pregnancy need extra food. Certainly they must have adequate protein, vitamins, calcium, and iron. But, because of fœtal anabolism, the pregnant woman is like a stove with the damper pushed in; less, not more, "fuel" is required. She must not consume too much carbohydrate, which (because of difficulty in oxidation or combustion) is not very suitable for a "damped-down stove." Only when all mothers, doctors, and midwives appreciate this shall we reduce toxæmia and eclampsia to near vanishing point; at present they rank as Public Enemy Number One in British obstetrics.

Reading. K. D. SALZMANN.

PAINFUL EXPERIMENTS ON ANIMALS

SIR,—Your report of July 27 (p. 195) of the recent House of Lords debate referred to the statement made by Lord Chesham, replying to Lord Dowding, that "many cases of cruelty had, however, been brought under the Protection of Animals Act, 1911, but no successful prosecution had ever been brought under it against anyone who held a vivisection licence."

For the accuracy of the record, may I refer to the fact that in 1946 there was such a conviction. Replying to a question in connection with this case in the House of Commons on Oct. 21, 1946, the then Home Secretary, Mr. Chuter Ede (see *Hansard* for that date) said that the person convicted "holds the certificates under the Act of 1876 authorising him to conduct certain experiments with a view to the study of nervous disease in man or animals. *He was convicted not for any offence in the performance of these experiments, but under the Protection of Animals Act, 1911*, for causing unnecessary suffering by keeping in a compound too many cats while they were suffering from distemper."

The National Anti-Vivisection Society, London, S.W.1. W. RISDON.

DIET AND CORONARY THROMBOSIS

SIR,—Without prejudice to the view that non-dietary factors may be of considerable importance, it seems to me that Professor Yudkin's data (July 27) are not altogether incompatible with a relatively simple correlation between diet and coronary mortality.

It seems that if the total fat intake is less than about 100 g. a day the mortality is low, irrespective of the kind of fat. If the total fat intake exceeds 100 g. a day there may be a high mortality from coronary disease depending on whether the diet contains a protective factor. This factor is apparently associated with certain vegetable and marine oils *including margarine*.

The countries for which Professor Yudkin gives statistics may then be divided into three groups. Using the numbering system given in his article, countries 12 to 15 fall into the low-fat category and consequently have a low coronary mortality. At the other extreme, countries 1 to 5 have a high fat intake and a low margarine consumption and thus have a high coronary mortality. Finland (4) has a total fat intake not greatly in excess of 100 g. a day, but falls into this category because of the low proportion of margarine or vegetable fat. The United Kingdom (6) has a relatively high coronary mortality as might be expected from a high total fat intake and a moderate margarine intake.

Inevitably, when dealing with statistics of this kind, there is a fairly large middle group—countries 7 to 11 with moderate coronary mortality and no dietary extremes, the relatively high fat intake in this group being balanced by a fairly high intake of vegetable fat or margarine.

It would be interesting to know the nature of the vegetable fat other than margarine consumed in some of the countries mentioned. For example, the United States (1) has a relatively high vegetable-fat figure, but a low margarine intake compared with Norway in which the margarine intake is high and the vegetable-fat figure is low.

Thus, contrary to what has generally been supposed, margarine would appear to have a significant amount of the protective factor.

There is some evidence that the protective factor is the essential fatty acids (E.F.A.). Professor Yudkin himself has pointed out that margarine may have an E.F.A. content five times that of butter.[1] The type of oil used for the preparation of margarine varies considerably from country to country and there may be a variation in the content of the protective factor. If margarine is, in fact, the hero and not the villain of the piece the prophylaxis of coronary disease by dietary means may be less drastic than some have envisaged.

Nottingham. R. COBB.

BLOOD-COUNTING MACHINE

SIR,—Reading the correspondence on this subject in your issue of Aug. 10 from the viewpoint of one instructed in and convinced of the fallacies of colour-index hæmatology, I share Dr. Shillitoe's downright attitude to the red-cell count and envy Dr. Watson-Williams the number of technicians he has to do his ever-increasing numbers of counts.

In this hospital, in addition to 250 antenatal screening hæmoglobins (which arrive in Wintrobe bottles), the number of individual-patient examinations and follow-ups dealt with in the cytological section averages 800 per month, and nearly all these are taken directly from the patient by the technical staff (including nearly 17% from practitioners' direct-service patients). Out of this total, hæmoglobin estimations are done in 664 cases. 264 white-cell counts are done. Blood-films are made in 712 cases (since every hæmoglobin and/or white-cell count requires a film). The rest of the examinations are: various (e.g., pleural and seminal fluids) 3%, and E.S.R.s alone 8%. This work is done by $2^1/_2$ technicians (as well as the prothrombins) and the films are read by the pathologist.

With the commercial advent of the red-cell-counting machines, we have had to decide whether or not to ask for one. Although we used to do some red-cell counts at clinical request, we have not seen advantage from these; and much confusion has arisen through colour-index calculations. Of course, we do not know whether we would not be better off with a really accurate red-cell count plus hæmoglobin plus film survey. We think we might be but, as Dr. Watson-Williams points out, we would need at least one skilled technician to operate and service the machine and cope with the numbers of counts. To us that would mean at least one extra technician for the same service we give at present.

Machines and technicians cost a lot, and where I differ from Dr. Watson-Williams, therefore, is in a present assessment of the likelihood of saving the cost of the machines. We feel we will have to wait until some larger laboratory equipped with money, time, and staff can really prove the benefits of having numerous red-cell counts (the white-cell counts do not matter so much, being quick and easy to do, not requiring a high degree of accuracy, and being readily checked by film survey).

After film reading we believe all films should be kept 5 years. Staining must have been reliable (e.g., May-Grünwald—Giemsa, not Leishman). Films are then packed back in the boxes in which they were sold, with microil left on, to avoid fading, scratches, and dust. A patient-follow-up file should be kept on at least a 5-year basis, with another file for special long-terms cases and, for example, leukæmias.

"Looking over the film," as Meynell puts it, takes, when one is learning, a long time for each film (particularly to establish which are really in all respects normal) and, when learning, this has to be done without reference to clinical

1. *Lancet*, 1956, i, 506.

problem or the hæmoglobin or white-cell figures. When the art is thoroughly learnt, however, bias can be avoided, and every figure and film is then assessed in relation to the current state of the case, on clinical information received. In this way the time towards diagnosis should be reduced to a minimum by the build-up of experience and data; and on such a basis the effect of the introduction of a red-cell-counting machine could be assessed.

Without such an assessment, calculating the numbers of counts one technician can do with a machine, and so estimating the value of the machine to patient and clinician would, I think, be fallacious; unless, of course, it is the total number of estimations alone which matters, and not their value in diagnosis, treatment, and after-care. Of the advantages of the mechanical counters where repeated and very numerous routine counts are a legal or moral necessity (as at Harwell) there is obviously no doubt. Of the advantages to a hospital laboratory we await the proof.

County Hospital,
York. G. A. C. SUMMERS.

CARDIAC ARREST DURING HALOTHANE ANÆSTHESIA

SIR,—Much of the correspondence on this subject has implied that a given percentage of halothane ('Fluothane') in the administered gases will be fatal, while other percentages are safe. While I am sure that such a peculiar idea never occurred to the writers, I would like to point out, explicitly, that it is false.

Narcosis depends on the concentration of the agent in and around certain C.N.S. cells; this is related to the blood concentration which is related to the alveolar concentration, and that in turn is related to the administered concentration—related, but never equal to, and only after a long time approximately so. The only available reading, therefore, which has any practical relationship to the level of anæsthesia is the blood concentration, and even this is a range—not a point.

The quantity of halothane required to achieve a given level of anæsthesia—that is to say, the actual number of grammes—varies widely from one individual to another. Whatever the amount may be, it can be delivered in a shorter time at a higher concentration, or in a longer time at a lower concentration. To speak of percentages of administered gases, or of settings of apparatus, without mentioning the duration and the state of the patient is meaningless.

It is accepted that 40% cyclopropane is a fatal concentration, yet it is also accepted that one may "fill the bag"—i.e., give virtually 100% cyclopropane—for a short time.

Similarly, one may advance the control of a Boyle mark-2 to the 6th notch (if the patient will tolerate it) without being guilty of poor technique.

For this reason I am afraid of halothane vaporisers delivering percentages as indicated on a gauge. An accurate vaporiser, delivering finely controlled, even increments is desirable—but so it is for any volatile agent.

If the vaporiser delivers given percentages, however, and the unskilled anæsthetist has a table of percentages, which, allegedly, give various levels of anæsthesia, one can foresee only a succession of fatalities and near fatalities in susceptible patients—to say nothing of the unsuccessful anæsthetics in resistant patients.

In short, mathematics, however essential preoperatively, has little place in the operating-room. With halothane, as with any other agent, a safe and successful anæsthetic demands a competent anæsthetist, using a machine and drugs he understands. He also needs some help from the Almighty, or, if you prefer it, luck.

Subdepartment of Anæsthesia,
Department of Surgery,
University of Ottawa,
Ottawa General Hospital. HAROLD T. KAY.

TRANSFUSION NOT TO BLAME

SIR,—Dr. Discombe's letter of Aug. 10 prompts me to record the following case:

A woman of 34, with a history of three normal confinements, had a normal pregnancy and delivery. An hour and a half after the birth there was a sudden uterine hæmorrhage of three pints of blood; her pulse became feeble and almost imperceptible, and her blood-pressure could not be registered. A request for blood was made; a technician collected several ml. of the patient's blood for matching. The serum was cherry red with hæmolysis. It was thought that the specimen might have been contaminated so I personally collected another sample using strict precautions. This sample also showed hæmolysis similar to the first. After this four bottles of blood were given; a bottle of fibrinogen was also given since hypofibrinogenæmia was present.

The next day the urinary output was greatly reduced, the urine being heavily stained with hæmoglobin; during the following days there was almost complete suppression of urine; the patient's condition deteriorated, the blood-urea and serum-potassium rose, and she died in uræmic coma on the ninth day. Sections showed a typical hæmoglobin-cast kidney.

Many cases of oliguria, some fatal, following abortion, incompatible blood-transfusion, or ante- or post-partum hæmorrhage, have been recorded.[1] In the case here recorded the intravascular hæmolysis is unexplained. If it had not been for the commendably acute observation of the technician who reported the hæmolysis, the tragedy would doubtless have been attributed to incompatible blood.

From a medicolegal point of view it is to be hoped that defence societies collect references to these cases. Coroners, the courts, lawyers, and the public assume that deaths following the use of the wrong blood are always due to that error and hold the laboratory worker or transfusionist responsible. Pathologists doing post-mortem examinations on subjects who have died under such circumstances should, I feel, never dogmatise except in affirming that the findings are consistent with natural causes or incompatible blood.

I wish to thank Dr. A. Bruce Cormick for permission to quote from the case-notes.

Worthing Hospital,
Sussex. R. AIDIN.

HEXYLRESORCINOL IN THE TREATMENT OF ARTHRITIS

SIR,—Rheumatic disease causes the loss of three million working weeks each year, at an annual cost of at least forty million pounds.[2] Enthusiasm for the use of gold and phenylbutazone has waned,[3,4] and the World Health Organisation's expert committee and other authorities have emphasised that drugs which give promising results should be investigated. I should like to record, therefore, some of my findings with 'Caprokol' (capsules containing 0·15 g. hexylresorcinol in oil) which I began to use in 1951.

The first case was a woman of 29 with rheumatoid arthritis who had been treated for over twelve months with cortisone, gold, salicylates, and physiotherapy. Her condition deteriorated, and she became bedridden. After five months' treatment with caprokol, 'Idolysin' (thiosinamine ethyl iodine), and ascorbic acid, she improved remarkably and was able to resume work She is now leading a completely active and normal life.

Since 1951 I have seen 215 patients with arthritis, and treated 165 (123 female and 42 male) on similar lines. The other 50 cases (40 female and 10 male) were used as controls. Of the treated patients, 62 had had salicylates, 25 cortisone, 44 gold, 16 penicillin, and 40 phenylbutazone—in no case with much improvement. The carpus was affected in 88, the knee in 76, the shoulder in 61, the hip in 49, the tarsus

1. Saltoun, D., Kinn, D. D. *Lancet*, 1957, i, 1280.
2. Peebles-Brown, R. A., Currie, J. P., Newbold, G. F., Ambrose, G. F. *World Hlth Org. tech. Rep. Ser.* 1954, 78, 2.
3. Peebles-Brown, R. A., Currie, J. P. *Brit. med. J.* 1953, i, 916.
4. Yeoman, W. *In* Medical Annual. Bristol, 1954; p. 358.

in 43, the elbow in 43, the wrist in 38, the ankle in 38, the spine in 15, and the temporomandibular joint in 2.

Treatment was as follows :

(1) Caprokol, 1–2 capsules four times daily, reducing to 1 capsule four times daily, on an empty stomach. A glass of milk was then given. There were no toxic effects.

(2) Idolysin 1–3 tablets (each containing thiosinamine 80 mg.) a day according to tolerance, and stopped at once if there was any sign of toxicity.

(3) Ascorbic acid 100 mg. three times daily.

The treatment was continued for five months, or longer if necessary.

Of 10 patients with grossly restricted movement of all limbs and the spine, all improved considerably. Similar improvement was seen in 23 out of 25 with the arms affected, in 9 out of 10 with the spine affected, and in both the patients with temporomandibular involvement. In all, of the 165 patients treated with hexylresorcinol, idolysin, ascorbic acid, and salicylates, 104 were much improved clinically, 50 moderately improved, and 11 not improved. Of the controls, none were much improved, 5 moderately improved, and 45 not improved.

Improvement was shown by relief of pain, increased ease of movement, reduction in localised œdema and tenderness, and (in some cases) radiological improvement.

The average decrease in joint circumference in the treated cases was $1^3/_4$–3 in. in the knees, $^1/_2$–$1^1/_2$ in. in the ankles, $^1/_2$–$1^1/_4$ in. in the elbows, and $^1/_4$–$1^1/_2$ in. in the metacarpophalangeal joints. No laboratory tests were possible because the patients were seen in general practice. Some patients, in both treated and control groups, needed special diets, rest, physiotherapy, corrective orthopædic measures, and control of focal infection and anæmia.

In most cases improvement was seen in three to five months. In some, joints became mobile though pain persisted; pethidine (50 mg.) was then given with benefit. Most of the patients were seen at monthly intervals for the first year and for review at three-monthly intervals for the second to fifth years. There was hardly any evidence of relapses.

I think the treatment worthy of further trial.

Liverpool. E. ALFRED LIPKIN.

A NEW DISEASE ?

SIR,—The article in the Widdicombe File (Aug. 10) on the origins of syphilis prompts me to record some observations by the late Prof. Haswell Wilson, while I was a medical student. He was discussing the theory that syphilis was first introduced into this country by the Crusaders; but added that there was evidence that the disease may have been described—although remaining unrecognised—in Old Testament times. He took the case of Samson, who had an amorous intrigue with Delilah. Thereafter, he lost his hair (alopecia), lost his strength (asthenia), and later developed blindness (keratitis or optic atrophy). Finally, he announced that he could demolish the temple unaided, thereby exhibiting the grandiose ideas of G.P.I.

Admittedly, Professor Wilson may have had his tongue in his cheek; nevertheless the possibility, however remote, of this being the earliest account of a syphilitic is interesting.

Bognor Regis, Sussex. A. F. ROBERTS.

SIR,—Dr. Irvine (Aug. 17) confounds us with four lines of Latin to make his point that the unfortunate shepherd was named Syphilus and not Syphilis. But surely Dr. Irvine in his turn perpetrates a further error in attributing the poem to one Frascatorius. Is not the accepted name of the author Fracastoro or, if one prefers the latinised form, Fracastorius ?

Department of Bacteriology,
Guy's Hospital Medical School,
London, S.E.1. C. G. A. THOMAS.

MORTALITY OF FRACTURES OF THE NECK OF THE FEMUR

SIR,—The exact toll of life taken by fractures of the neck of the femur is not the least of the effects of this increasingly common injury. In a recent review [1] reference is made to the lack of comparable statistics from a true sample of the ageing population. A mortality is quoted of between 23% and 28% for 150 patients of an average age of 78 years, and it accords accurately with another recent survey.[2] Both these figures in turn agree with those for the total incidence of the injury in this area.[3] The original analysis has now been extended to cover four years during which time a total incidence of 388 cases, of an average age of 77 years, suffered a mortality of 28·6% within the first six weeks.

A mortality of only 16% has been quoted.[4] This low figure can represent but part of the sum total who die following these injuries. Such disparities, however, serve to underline the need for a more precise assessment of all the implications of this common problem.

Dundee. I. M. STEWART.

INDUCTOTHERM IN ANURIA

SIR,—Five long days of anuria followed catheterisation of a young man's only remaining ureter. After many unrewarding attempts at inducing diuresis I remembered being told [5] of an anuria which had ceased soon after short-wave treatment to the patient's loins.

Accordingly I asked a physiotherapist, Miss M. Mack, to help: she placed a pancake coil from an inductotherm over the kidney area and gave a comfortable heat for quarter of an hour. Straightaway a great diuresis set in and thereafter a good flow has continued to the present, three years later. If this was coincidence only, it was a happy one; and perhaps someone, having tried the usual methods, may be glad to be reminded of the inductotherm.

Launceston, Tasmania. W. W. WOODWARD.

UNNECESSARY IRRADIATION IN CHEST RADIOGRAPHY

SIR,—Though a larger area of the body may be subjected to irradiation than is necessary at most investigations it would seem that more harm is done by thoughtless unnecessary multiple radiographs. It is the radiologist who is most exposed to the dangers. I have witnessed the agonies over years and subsequent deaths of two colleagues from malignant disease and have tried to get my clinical colleagues to appreciate the dangers to which they subject the X-ray staff by their demands. Your correspondent "Radiologist" (Aug. 17) refers to the neglect of the clinical examination. Far too many radiographs are demanded for checking—the intervals between are often too short to permit of any other report than "No change," a report that does the patient far more harm and certainly contributes far less to a knowledge of the condition of the patient than a careful clinical examination. I have complained at finding more than 100 radiographs of a chest, and of a limb with a fracture.

With the facility to call on the Government to bear the expenses there has been an undue demand for investigations and with these an exaggerated demand for staff, equipment, accommodation, &c., but the damage to the patients and workers produced cannot yet be estimated—the expenses incurred ought to have checked the abuse.

1. Soutter, F. E., Smith, D. H. *Lancet*, Aug. 3, 1957, p. 204.
2. Murray, D. B., Young, S. *Ibid*, 1957, i, 597.
3. Stewart, I. M. *Brit. med. J.* 1955, i, 698.
4. Newman, P. *Lancet*, 1957, i, 689.
5. Mallam, P. C. (1948) Personal communication.

Was it necessary for Mr. Clarke, whose article appeared in your issue of Aug. 17, to take 3 radiographs of a patient to demonstrate what has clearly been indicated by the article by Ardran which he quotes? Was it not unnecessary irradiation?

If the propaganda about the dangers of irradiation continues with its exaggerations we shall soon find it difficult to get any workers in X-ray departments; but if that leads to an improvement in clinical methods it could be claimed to have done a good service.

The criticism which Dr. Thomas Addison made of the stethoscope can be much more truthfully applied to the X ray, as I have indicated.[1]

Birmingham, 15. JAMES F. BRAILSFORD.

CONSULTANT AND SPECIALIST

SIR,—"Senior Registrar" asks (Aug. 17) if the Ministry of Health has rejected any applications for the creation of a new consultant appointment. I can report two happenings at one teaching hospital.

A special reference clinic was proposed. I was told I could have a room and a nurse but it would be no good asking to be paid for the extra session a month. (The need for such a clinic is shown by one having developed a waiting-list of 5 months, despite having 2 consultants and doing 2 or 3 sessions a month.)

Two years ago the medical committee recommended a new consultant appointment for 4 sessions a week. After about a year the Ministry approved such an appointment but said they would make no extra allotment of moneys to pay him (which seems to me rather dishonest behaviour).

TEACHING-HOSPITAL CONSULTANT.

WOMEN IN PRISON ON "ATTEMPTED SUICIDE" CHARGES

SIR,—Dr. Epps (July 27) touches on the problems presented by suicidal alcoholics.

She found 24 "chronic alcoholics" among 100 women on "attempted suicide" charges. This is a slightly higher proportion than usually reported among suicidal women, where the percentage of alcoholics has been said to range between 3 and 12 (average 8); among suicidal men, alcoholics formed a proportion of between 25 and 40% (average 30).[2] Figures also seem to vary a great deal if, instead of asking for the frequency of alcoholics among "attempted suicides," one investigates the question of how many alcoholics have made suicidal attempts. Thus, in a large German study, of the alcoholics admitted to a university clinic, about 4% of the men and 4·5% of the women had attempted suicide.[3]

Figures in recent years in this country seem to show that suicidal attempts are not uncommon among alcoholics of all social classes. Thus, a quarter of the middle-class alcoholics (predominantly occupational groups I and II) seen at Warlingham Park Hospital had a history of suicidal attempts (24% of 200 men, 26·5% of 68 women). Among a series of 56 male and female alcoholics recently admitted to a London observation ward—the majority belonging to occupational groups III–V—12 (21%) had attempted suicide in the past.[4] Finally, among homeless men admitted to a London observation ward—mostly occupational groups IV and V—out of 40 in whom alcohol consumption had been excessive, 13 (33%) gave a history of suicidal attempts, as against only 11% among 90 men who had not been heavy drinkers. Of the 40 heavy drinkers, 15 were classified as alcoholics; 4 of them had attempted and 4 threatened suicide.[5]

Alcoholism is regarded by some as "chronic suicide,"[6] by others as an "avoidance of suicide," the alcoholic turning to suicide only when alcohol intoxication fails to blot out the undesirable aspects of life.[7] The relative frequency of suicidal attempts among alcoholics is easily understandable in the light of those hypotheses which regard social isolation[8] and the loss of the inner feeling of identity with a recognised social grouping ("subjective excommunication")[9] as highly important factors in the genesis of suicidal attempts. Such experiences must be very common and severe in the case of alcoholics, whose behaviour leads to "a progressive withdrawal from the social environment" and to a "system of isolation."[10]

According to a recent American review of alcoholism and suicide, "those who are psychopaths or depressives are more likely to try this way out."[2] A third of Dr. Epps's series of 24 alcoholics were "psychopathic." Among the W.P.H. alcoholics a history of suicidal attempts was relatively more common in psychopaths (33% of 86 men and women) than in non-psychopaths (21% of 182 men and women), younger age-groups (21–40 years) predominating among the suicidal psychopathic alcoholics, older ones among the non-psychopaths.

Of the suicidal women described by Dr. Epps, most had gone to a general hospital after their suicidal attempt but had stayed there for only a very short time. One reason for this, according to Dr. Epps, is that "some of them—usually the alcoholics and psychopaths—can be a nuisance to those around them, and may be unwelcome in both general and psychiatric wards." According to Dr. Epps the non-psychotic alcoholics seen by her "might or might not be treatable." In general it would probably be fair to say that at least some of the 10 "psychoneurotic" alcoholics in her series—seeing that the great majority were of at least average intelligence—should have some chance of improving under treatment, and that if treated in the setting of an alcoholic group within the hospital, these (neurotic) patients would not prove a nuisance.

The problem of the treatment of alcoholic offenders is also touched upon in your annotation (July 27) on a report on some recent suggestions by the Advisory Council on the Treatment of Offenders. The council agreed that in the case of the "chronic alcoholics" their "offence suggests that prison is prima facie unsuitable and useless"; but it could see no alternative at present to imprisonment, though occasionally probation and residential treatment might be tried. The council reports that very few of the alcohol addicts seen in prisons are of suitable character and intelligence for psychotherapy. But occasionally a more intelligent type of alcoholic, responding to psychotherapy, must turn up in prisons, as is evident from the fact that more than a fifth of the W.P.H. alcoholics had been in prison (and another third before the courts) at some time before hospital admission. Anyhow, facilities for the residential treatment of alcoholics outside prisons are very scarce, and, where present, their permissiveness makes them not very suitable for the treatment of aggressive psychopathic alcoholics. As the council did not suggest any alternative to imprisonment, the question arises whether more could not be done for these people while in prison. The council reports that prisoners are allowed to make contact with Alcoholics Anonymous, but (in contrast to the United States) there are as yet apparently no A.A. prison groups in this country. A great number of the prison alcoholics must be psychopaths who may easily disrupt such a group[11][12] though it might be expected that the group would be able to "carry" a few psychopaths. It might, therefore, be more advisable to have the alcoholic prisoners "screened" by a psychiatrist and to create separate (and perhaps psychotherapeutic) groups for non-

1. *Radiography*, June, 1957, p. 157.
2. *Conn. Rev. Alc.* 1955, **7**, 14.
3. Graute, P. *Allg. Z. Psychiat.* 1939, **111**, 47.
4. Fleminger, J. J., Glatt, M. M. To be published.
5. Glatt, M. M., Whiteley, J. S. *Mschr. Psychiat. Neurol.* 1956, **132**, 1.
6. Menninger, K. A. Man Against Himself. New York, 1938; chapter 3.
7. Haggard, H. W., Jellinek, E. M. Alcohol Explored. New York, 1950; p. 162.
8. Sainsbury, P. Suicide in London. Maudsley Monographs No. 1. London, 1955.
9. Strauss, E. B. *Brit. med. J.* 1956, ii, 818.
10. Alcoholism subcommittee (2nd report). *Wld Hlth Org. tech. Rep. Ser.* 1952, **48**, 34.
11. Slavson, S. R. (editor). The Fields of Group Psychotherapy. New York, 1956; chapter 1.
12. Pfeffer, A. Z., Friedland, P., Wortis, S. B. *Quart. J. Stud. Alc.* 1949, **10**, 198.

psychopathic and psychopathic alcoholics. Prison treatment would possess at least one advantage in that these alcoholics could be approached while sober, for sobriety is harder to obtain and maintain in a severely psychopathic alcoholic in a very permissive atmosphere. The results from such an approach might not be overwhelmingly good, but some improvement could at least be expected in the non-psychopathic offender of average intelligence.

Warlingham Park Hospital, Surrey. M. M. GLATT.

A CLINIC FOR HOMOSEXUALS

SIR,—Ever since the celebrated case in 1954 the subject of homosexuality has been simmering in the public mind. The report of the Wolfenden Committee is expected shortly and its publication will bring the matter to the boil again.

Much research has been done, and must continue to be done, into the causes and possible cure of homosexuality, but the fact remains that there are a great number of established homosexuals, perhaps not far short of a million, in this country today. This number will not change if the law is changed. Homosexuality will still be a problem, both to society and to the individual. A change in the law, should it be recommended and carried through, must never be interpreted by the public as meaning that the problem is no longer of any significance beyond its relation to young people and to public decency. Certain it is that homosexuals will go on having their trials and tribulations (perhaps more, perhaps less, who can tell?).

Existing opportunities for a homosexual to obtain help are limited. The medical profession as a whole has unfortunately been unable over the years to dissociate itself from the distaste with which the general public views the matter. Consequently there has been confusion of thought and practice, confusion too easily conveyed to the homosexual seeking help. He is often reluctant to consult his own doctor who, he believes, is unlikely, because of prejudice or ignorance, to be able to understand him. This is a sorry state of affairs, and while there are indeed some outstanding experts on the subject, the paths to their consulting-rooms are not well signposted.

A few months ago a feeler was put out to assess the reaction of some fifty men and women, in all spheres and walks of life, to the idea of setting up a clinic to be devoted exclusively to homosexuality and its related problems. The reaction was overwhelmingly favourable, and at a meeting in June, attended by twenty people (nine of whom were doctors), a proposal that the project was valid, was worth undertaking, and deserved support was carried unanimously.

Although there is still much preliminary work to be done before the clinic can come into operation, it is felt that a great many doctors will be interested to know of the project at this stage. The primary aim is clear: it is to decrease the magnitude of the homosexual problem. The clinic will be run on an outpatient basis in a convenient part of London. It will offer no new therapeutic technique except in so far as a clinic concerned solely with homosexuals is new, and this may well prove to be a big step forward.

The objectives of therapy are only touched upon briefly here. For the young who have encountered difficulties on the road to maturity, and for the adults who have a bivalent sexual instinct, the objective will be adjustment to heterosexuality. For the people in whom any heterosexual urge has always been absent and will never, humanly speaking, be present, the objective will be better adjustment to homosexuality, thereby releasing, for the benefit of the community at large, the great potential for good work which so often lies dormant in homosexuals. There are certainly well-adjusted homosexuals whose contribution to society must be rated very highly.

The clinic will also act as a centre for the spread of knowledge. Research will be carried out concurrently with therapy, which will include group therapy conducted under proper medical supervision; the scope in this direction is considerable. To start with, at all events, the project will have to be financed by funds raised by private subscription, but it is hoped that the clinic will become self-supporting.

The general interest and support of the medical profession is sought for this project, which represents a sincere attempt to tackle a serious problem. The Church and all responsible bodies are anxious and willing to play their part but, on the admission of everyone seeking to enlighten the shadows of homosexuality, medicine's contribution is the most vitally important.

Hurst Green, Surrey. RODNEY H. N. LONG.

DIHYDROCODEINE

SIR,—Following the interesting letter from Dr. Swerdlow,[1] a study has been made at this hospital of the intravenous use of dihydrocodeine þitartrate as an analgesic adjunct to thiopentone/nitrous-oxide anæsthesia. It has been found that satisfactory analgesia is obtained without significant side-effects and, in order to investigate the range of possible dosage, increases were made in cautious steps. It was found that for an average adult a satisfactory initial dose lies between 20 and 35 mg. in an 0·5% solution shortly after induction with thiopentone sodium, and that when higher doses in the region of 100 mg. were given obvious and undesirable side-effects occurred. Marked falls of blood-pressure were observed, even to unrecordable levels, and respiration was depressed to the point of apnœa. In addition there appeared a generalised erythema whose cause has not yet been established. Rapid recovery followed the administration of oxygen by intermittent compression of the rebreathing bag, intravenous nalorphine and methylamphetamine, and tilting the patient into the head-down position.

It must, however, be emphasised that 100 mg. of dihydrocodeine is approximately equivalent in analgesic potency to several times the usually accepted intravenous dose of pethidine hydrochloride. Dihydrocodeine is proving a most useful analgesic, both during anæsthesia and postoperatively. Within its optimal range of dosage it can be administered repeatedly even during prolonged anæsthesia, yet is notably free from side-effects.

St. George's Hospital Medical School, London, S.W.1. JACK LEVIN.

EFFECT OF CERTAIN PROTEIN FOODS ON BLOOD-SUGAR LEVELS AND GLUCOSE TOLERANCE

SIR,—The extremely interesting and clinically promising article by Dr. Srinivasan (Aug. 17) may be related to the clinically important, though perplexing and seldom mentioned, different effects of hot and cold meat on the development of hypoglycæmia. Patients who take soluble insulin before dinner in the evening and then eat hot or re-heated meat, be it beef or mutton or ham, are less prone to develop hypoglycæmia late at night than when they eat the same amount of cold meat. Possibly similar to this is the mild or even severe hypoglycæmia in normal people about noon or at tea time after eating an uncooked breakfast or lunch, and the prevention of this hypoglycæmia by a breakfast or lunch of fried bacon or hot meat.

London, W.1. FRANKLIN BICKNELL.

1. Swerdlow, M. *Lancet*, 1957, i, 482.

THE STATE OF DEVELOPMENT OF NEWBORN AFRICAN CHILDREN

SIR,—Dr. Tanner's excellent letter of July 27 encourages me to carry his point perhaps a little further.

He refers to some of the work showing that African and Negro children are more advanced in skeletal maturity in early life than white American and European infants; and "their advancement in respect of skeletal maturity either depends on 'intrinsic differences' or else on differences in prenatal environment, and the former is certainly the more probable." I agree absolutely but I think we need more evidence in problems of this kind. It is frequently assumed that environment only "starts to act" at the moment of birth; clearly it can in fact be so bad before this moment that the child does not survive to reach it. Studying detailed prenatal environment is obviously fraught with difficulty and evidence is hard to come by, but in the past it has rarely been sought.

In a recent study [1] we have demonstrated this advance of Negro over white babies, but also that the well-known and usually found advance of the female over the male in skeletal maturity during childhood of white children is not present in a sample of West African children up to two years. This I regard as supporting Dr. Tanner's evidence that there are certain basic intrinsic differences between Negro and white children regarding early growth patterns.

We demonstrated, too, that the African babies' growth *rate* was significantly more rapid in the first six months than certain comparable European samples living in Europe. This may well be due to an unlimited supply of breast-milk or other environmental factors at this time, for this advance falls off after one year. This last observation brings me to a final point: Dr. Tanner gives the impression (only by his use of "either," "or," and I know he will forgive the friendly barb) that effects of this kind are either intrinsic or environmental. Both factors are, in fact, irrevocably inseparable and capable of interaction. To estimate the weightings of each, in, for example, my last example, is a highly complex business.

Child Development Unit,
Department of Pediatrics,
University of Louisville,
Kentucky.

FRANK FALKNER.

ILEOSTOMY CHEMISTRY

SIR,—Dr. Abbott and his colleagues (July 20) have been kind enough to draw attention to the most important feature in our findings—namely, that during the first three to five days after a newly established ileostomy begins to act sodium may be excreted at approximately 300 m.eq. per litre during a 24-hour period. By recent ileostomy we refer particularly to this period, since after a week the concentration falls. From 6 recent ileostomies the concentration was 300 m.eq. per litre or more during one or more days in 3 cases, 400 in 1, and approximately 200 in 2. We agree that these figures must be treated with reserve until they are confirmed. Unfortunately no similar studies seem to have been published for comparison. The figures quoted by Dr. Abbot from Lockwood and Randall [2] appear once in one table and no indication is given as to how they were obtained, or how soon after operation, whether one patient or more was studied, or over how long a period collection was made. Samples were obtained in cases of paralytic ileus or mechanical obstruction by Dr. Abbott and his colleagues; these are circumstances hardly comparable with our own. Dr. Coghill and his colleagues [3] have published figures under conditions closest to those with which we were working; comparison can only be made with two of the cases they quote and since they measured output in grammes the assessment of concentration of sodium in the output is difficult.

We appreciate that total sodium loss cannot be properly assessed unless full sodium-balance studies are undertaken, and this we are doing now. Nevertheless we noted that there was no definite reciprocal relationship between urinary and ileostomy sodium losses. We therefore thought it useful to state that there was no clear evidence of urinary conservation of sodium.

As regards potassium needs we intended to imply that we were referring to replacement of loss from the ileal stoma. We thought that this would be inferred from the text and that clinicians applying our figures would take into account other factors such as renal loss when assessing the total need, without specific mention by us. We regret that by not making this abundantly clear we have caused misunderstanding.

Queen Elizabeth Hospital,
Birmingham, 15.

N. CRAWFORD
B. N. BROOKE.

RADIATION AND LEUKÆMIA

SIR,—In his letter of July 27, Dr. Mole points out that the data obtained in our study of irradiated spondylitis [1] appear to show that the susceptibility to the induction of leukæmia varies with age and he asks whether the form of standardisation which we adopted in assessing the relationship between dose of radiation and the resulting incidence of leukæmia was adequate to take account of this variation. In a desire to keep the report as brief as possible we did not publish the whole data separately for each age-group and it has, therefore, been impossible for other workers to test the adequacy of the method of standardisation for themselves. We regret this and have now attempted to correct it by duplicating the full tables; we will be pleased to send copies to anyone interested in them.

In view of the considerable difference in the rate of induction of the disease observed in different age-groups, it would clearly have been preferable to study the dose-response relationship among patients who were all of the same age. Our material was, however, so limited that it seemed likely that any attempt to do this would introduce greater errors due to chance variations in the small numbers of cases observed, than would be introduced by analysing the whole material and attempting to correct for the variation in susceptibility by standardisation. The method of standardisation adopted was an indirect one and, in certain circumstances, this may be less efficient than the direct method. The direct method, however, has the disadvantage that errors due to chance variation in the numbers recorded in small groups are likely to be grossly exaggerated and the results may, in consequence, be disproportionately distorted. Any form of standardisation is a somewhat artificial procedure and different results may always be obtained by choosing different populations as the standard. Fortunately such differences are usually slight and seldom affect the general trend of the results. In the present case, the results obtained by different methods of standardisation are all compatible with the hypothesis that, at low levels of dose, the incidence of the disease is directly proportional to the dose of radiation received. A comparison is shown in the accompanying table between the results obtained by (1) the indirect method of standardisation used in the report, (2) the direct method using the age-distribution of the whole irradiated male population as a standard, and (3) limiting the analysis to the age-group of 25–44 years, within which there did not appear to be any substantial variation of incidence with age.

1. *Proc. Amer. Ass. phys. Anthrop.* April, 1957.
2. Lockwood, J., Randall, H. T. *Bull. N.Y. Acad. Med.* 1949, **25**, 228.
3. Coghill, N. F., Lubran, M., McAllen, P. M., Edwards, F., Richenberg, C. S. *Gastroenterologia*, 1956, **86**, 724.

1. Court Brown, W. M., Doll, R. *Spec. Rep. Ser. med. Res. Coun., Lond.* 1957, no. 295.

INCIDENCE OF LEUKÆMIA AFTER DIFFERENT MEAN DOSES OF THERAPEUTIC IRRADIATION TO THE SPINAL MARROW (RATES PER 10,000 MEN PER YEAR)

—	Estimated rate in absence of therapeutic irradiation	Mean dose to spinal marrow (r.)					No. of cases of leukæmia
		Less than 500	500–999	1000–1499	1500–2249	2250 or more	
Standardised for age by indirect method ..	0·49	1·98	4·66	7·21	14·44	72·16	37
Standardised for age by direct method ..	0·49	2·25	4·75	7·34	11·21	97·44	37
Analysis confined to ages 25–44 yr. at first treatment	..	2·70	2·59	5·73	13·60	27·06	20

The results shown in the table (and to which Dr. Mole referred) are obtained from an analysis of the data for all the patients in our series, irrespective of whether they received spinal or extraspinal irradiation. In our view the most useful results are those which were obtained by limiting the analysis to the data for those patients who received spinal irradiation only. Substitution of a direct method of standardisation for an indirect one does not materially modify these results and leads to an estimate of 95r for the dose to the spinal marrow which would double the incidence of leukæmia against the value, estimated in our report, of 94r.

W. M. COURT BROWN
RICHARD DOLL.

London, W.C.1.

THE NEWBORN INFANT'S OXYGEN-SUPPLY

SIR,—We have been interested in the recent articles and lively correspondence debating the issue of delayed versus early ligation of the umbilical cord as a means of preventing hyaline-membrane syndrome.

It occurred to us that the fate of twins is relevant to this debate. Seip [1] has shown that the second-born twin usually has a higher hæmoglobin and erythrocyte-count than the first-born twin, during the first two weeks of life. This discordance is assumed to result from an extra "blood-transfusion" as a consequence of relatively delayed clamping of the cord and more complete contraction of the uterus when the last born fœtus is delivered.

Accordingly we examined the retrospective experience of the premature nursery of Babies Hospital. 1875 premature infants whose birth-weight was less than 2000 g. were admitted to this unit in the past seven years. Complete necropsies were performed on 30 sets of twins (both individuals of the pair died) who succumbed before the age of four days. An almost identical incidence of hyaline membrane was noted.

	1st-born twin	*2nd-born twin*
Hyaline membrane	7	8
No hyaline membrane	8	7
Total	15	15

The necropsy experience with all twinned individuals (not pairs) who died before the age of four days revealed the same result.

	1st-born twins	*2nd-born twins*
Hyaline membrane	12 (*41%*)	15 (*41%*)
No hyaline membrane	17	22
Total	29	37

Though it may seem that the subject of hyaline membrane is confused enough without considering this additional imponderable, we believe that it is pertinent to bring these observations to the attention of the debaters.

WILLIAM A. SILVERMAN
MASAKO NISHIHARA.

Babies Hospital,
New York.

1. Seip, M. *Acta pædiat.* 1956, **45**, 58.

PENICILLIN TREATMENT OF LEPTOSPIROSIS

SIR,—Following the publication of Fairburn and Semple's article in your columns last year [1] (which concluded that "penicillin and chloramphenicol play no useful part in the treatment of uncomplicated leptospirosis in British troops in Malaya and we suggest that these antibiotics are unlikely to be of value in the treatment of leptospirosis elsewhere"), I wrote a short letter [2] in which I related my favourable experience of penicillin in the treatment of that disease. Major-General Drummond [3] replied that "the views expressed last week by Captain Clein are to be respected in that they represent his own personal opinion. I feel I should point out, however, that at present the weight of specialist opinion in the Army Medical Services is that penicillin is of little value in the treatment of leptospirosis as encountered in Malaya and Singapore." It is gratifying therefore to see that Lieut.-Colonel Mackay-Dick and Captain Robinson (Aug. 17), using almost exactly the dosage schedule of penicillin I recommended in the treatment of leptospirosis, have obtained almost identically favourable results as I did.

My series of 20 successive cases occurred in Commonwealth troops serving in Malaya, and were treated at the British Military Hospital, Kluang, Johore, between May, 1954, and August, 1955.

The nationalities of the patients were Gurkhas (7), Fijians (8), British (4), and Malay (1). The dosage of penicillin employed was 600,000 units four-hourly for five days, treatment being commenced as soon as the clinical diagnosis was made. All these 20 cases were later confirmed serologically. All the cases were fever-free within forty-eight hours, and indeed 14 were apyrexial within twenty-four hours.

The average length of stay in hospital was only fourteen days—before transfer by a lengthy journey to an active convalescent unit. There were no deaths in the series. In fact so dramatic were the results obtained by penicillin treatment that I much doubted the diagnosis if a case suspected as having leptospirosis and treated with penicillin was not considerably improved within twenty-four hours. Colonel Mackay-Dick and Captain Robinson state that in no case in their series did polyuria or low-specific-gravity urine develop. Indeed, in my series 3 cases failed to develop any detectable renal changes whatsoever.

Why were the results obtained by Fairburn and Semple so different from these two series? The answer may be quite simple. The dosage of penicillin employed by them was only 2,400,000 units daily in comparison with 3,600,000 units daily in my series. Possibly the dosage employed by them was inadequate.

It would be interesting to know what the weight of specialist opinion in the Army Medical Services now is regarding the treatment of leptospirosis.

The Maudsley Hospital,
London, S.E.5.

LEWIS CLEIN.

HIGH-PRESSURE OXYGEN AND RADIOTHERAPY

SIR,—Dr. Targowsky (July 27) suggests that it might be possible to increase tissue oxygen tension by intra-arterial blood-transfusion. This would be true only if the added blood contained oxygen at a higher tension than that in the arterial blood. The method would thus involve the use of an artificial lung, and even so the transfused blood would form only a part of the resultant arterial stream.

As the oxygen tension in the arterial blood closely approximates to that in the alveoli it seems simpler to raise it by increasing the oxygen-tension in the inspired gases, and this is the basis of the technique we have used. For reasons discussed in detail elsewhere [4] it seems likely that

1. *Lancet*, 1956, i, 13.
2. *Ibid*, p. 289.
3. *Ibid*, p. 297.
4. Churchill-Davidson, I., Sanger, C., Thomlinson, R. H. *Brit. J. Radiol.* 1957, **30**, 403.

the inhalation of pure oxygen at pressures higher than one atmosphere is needed to restore some suboxygenated tumour cells to the radiosensitive state. We used anæsthesia to reduce the risk of oxygen convulsions and for the patients' comfort; our technique may appear complicated and even hazardous but in fact very few practical difficulties were encountered.

If one had a pressure-chamber large enough to admit an attendant, and patients trained to tolerate compression, complete anæsthesia (and myringotomy) might be unnecessary. The practicability of such an arrangement for the treatment of numbers of unselected patients is being actively considered. Auler et al.[5] used this method in 1929 for the treatment of cancer. They did not irradiate their patients and achieved no success with oxygen alone.

Although altering the arterial oxygen tension is probably the most direct way of influencing tissue oxygenation, two other possible methods are worth considering. The first is to increase the blood-flow so that there is a smaller drop in oxygen tension between the arterial and venous ends of the capillaries; this may be what Dr. Targowsky had in mind, though it is doubtful if intra-arterial blood-transfusion would achieve it. The second is to alter cellular metabolism so that less oxygen is consumed. These approaches may eventually prove fruitful; for the moment they lie on the fringe of possibility.

Department of Anæsthesia,
Hartford Hospital,
Hartford, Connecticut. CYRIL SANGER.

REFLECTIONS ON MEDICAL TRAVEL

SIR,—It was with particular interest that I read Prof. Witts's article.[6] There are, however, certain points which I would like to clarify.

Professor Witts writes that peptic ulcer and lung cancer are common in Burma but uncommon in North India and Pakistan. While it is true that the prevalence of peptic ulcer is insignificant in the Punjab, the frequency of this illness is almost alarming in East Pakistan and the southern region of West Pakistan. This may partly be explained by the relatively poor standard of living in these regions as compared with the Punjab, where special emphasis is traditionally placed on rich and good diet. Peptic ulcer is so common a disease in East Pakistan that partial gastrectomies occupy a fairly prominent place on the operation-lists. Lung cancer is not so uncommon as Professor Witts has suggested. In big cities where Western civilisation is holding its sway and people are getting more and more into the habit of smoking, the incidence of lung cancer is fairly high. Religious and social prejudices towards necropsy have added to the difficulties of assessing the true incidence. In the countryside, however, the disease is uncommon. The villagers are usually in the habit of smoking hooka or biri, which are probably free from any carcinogenic substance. Cigarette-smoking in villages by the way, is thought to be a social curse, and this may explain the lower incidence of lung cancer—if, of course, cigarette-smoking is to be incriminated as the cause of the colossal rise in lung cancer in recent years.

Leukæmias are almost a rarity in Pakistan. In our hospital, I have seen only 3 cases during the past three years. Parenchymatous syphilis is, curiously enough, a rarity. I have so far never seen a case of tabes dorsalis or general paralysis of insane. Disseminated sclerosis, however, one encounters occasionally. Cirrhosis of the liver is perhaps one of the commonest diseases in Pakistan. The usual variety in this part of the country is post-necrotic, diffuse hepatic fibrosis being fairly uncommon. This is probably because the diet of the common man lacks all the essential proteins and lipotropic factors. Death in cirrhosis of the liver is usually due to liver failure or intercurrent infection. Hæmatemesis as the terminal event is not so common. Carcinoma of the liver is very common. The liver cancers are usually primary carcinoma (hepatoma). This high incidence may in part be due to the prevalence of cirrhosis, or some nutritional deficiency may be responsible for both the carcinoma and cirrhosis, for liver cancer is almost confined to cirrhotic livers.

Clinical experience points to the occurrence of malignant change in patients already suffering from cirrhosis of liver rather than malignant change in normal livers. Rapid worsening of the patient's clinical condition, rapid and tender enlargement of the liver, fever, and the appearance of obstructive jaundice in this country in a patient known to have cirrhosis of the liver almost invariably indicate that malignant change has supervened.

Liaquat Medical College,
Hyderabad, W. Pakistan. ALI MUHAMMAD.

VITAMIN SUPPLEMENTATION

SIR,—All will agree with Prof. Moncrieff (Aug. 17) that dairymen's orange juice is almost valueless as a source of vitamin C and that infants who receive it are at risk from scurvy. The disquiet which I felt on this account was allayed, however, when I discovered that only 3 (1 at eight months and 2 at ten months) of the 1313 infants in the Luton inquiry were being given dairymen's orange juice. In addition, 3 infants (1 at ten months and 2 at eleven months) were receiving proprietary fruit-squash drinks which, for want of evidence to the contrary, were also disregarded as sources of vitamin C.

Public Health Department,
Luton. R. M. DYKES.

GENERATION DEATH-RATES AND TUBERCULOSIS

SIR,—There has been much discussion recently of the generation death-rates [1–3] and their application to the study of tuberculosis.[2 4–6]

As has been pointed out by several authors, if a biologist had complete control of a colony of short-lived animals, he would naturally use generation death-rates in the study of, say, an infectious disease. The notion of constructing a life table in the customary manner from the death-rates is sophisticated and does not come naturally to mind. Andvord [7] apparently had such a biological view of the study of tuberculosis in a human community over a long period; for he cites an earlier statement: "Bearing in mind the latent period, there are compelling reasons why we should fix as the time of infection the infantile years for the great majority of the tuberculous diseases, and the fœtal period only for an inconsiderable number of cases." [8]

Moreover, Andvord [7] believed that such a study would be appropriate in other diseases and cites Lie,[9] who had concluded that leprosy was best considered as an infective disease of infancy. That his views were considered novel can be seen by reading Elderton's review [10] of Andvord.[7] Andvord [4] introduced a study by generations of the tuberculosis death-rates. Frost [5] saw that this approach gave an explanation of the change in the form of the graphs of the death-rates from tuberculosis examined at a particular year. Frost apparently did not know of the works of Derrick,[11] Davidson and Reid,[12] or Knibbs.[13] Case,[1] however, goes so far as to deny that Derrick was considering generation death-rates. This seems to be incorrect and Derrick appears to have had some influence on other actuarial writers such as Tayler [14] discussing the paper of Laing.[15] Tayler thought that generation life tables should

5. Auler, H. H., Herzogenrath, H., Wolff, B. *Z. Krebsforsch.* 1929, **28**, 466.
6. Witts, L. J. *Lancet*, 1957, i, 1291.

1. Case, R. A. M. *Brit. J. prev. soc. Med.* 1956, **10**, 159.
2. Springett, V. H. *Lancet*, 1952, i, 521, 575.
3. Daw, R. H. *J. Inst. Actuar.* 1950, **76**, 143.
4. Andvord, K. F. *Norsk Mag. Laegevid.* 1930, **91**, 642.
5. Frost, W. H. *Amer. J. Hyg.* 1939, **30**, A91.
6. Springett, V. H. *J. Hyg., Camb.* 1950, **48**, 361.
7. Andvord, K. F. *Tubercle*, 1921, **3**, 97.
8. Andvord, K. F. *Norsk Mag. Laegevid.* 1895 (cited by Andvord, footnote 7).
9. *Arch. Derm. Syph.* 1911, **110**, 780 (cited by Andvord, footnote 7).
10. Elderton, W. P. *Biometrika*, 1922, **14**, 191.
11. Derrick, V. P. A. *J. Inst. Actuar.* 1927, **58**, 117.
12. Davidson, A. R., Reid, A. R. *Trans. Fac. Actuar.* 1928, **11**, 183.
13. Knibbs, G. H. The Mathematic Theory of Population. Appendix A. Census of the Commonwealth of Australia, 1911. Melbourne, 1917.
14. Tayler, H. H. In discussion on Laing (footnote 15).
15. Laing, J. M. *J. Inst. Actuar.* 1928, **59**, 125.

be constructed for the past generations in England; he made the observation that the shape of the curves of q_x on a generation basis had not changed as much as had the curves of q_x on a calendar basis.

? The first, however, to give explicit mention to a generation method may have been Cherry,[16] who was interested in studying the coincidence, first presumably noted by Coghlan,[17] whereby the sum of the cancer and tuberculosis death-rates was almost a constant in the New South Wales experience and about 20% of all deaths above the age of 15 years were due to cancer and tuberculosis combined. Cherry saw that this problem would best be considered on a generation basis, as we should now say. His tables 6 and 7 are prototypes of fig. 1 of Case [1] and table 14 of Springett.[6] Cherry gives acknowledgment to Sir Thomas Lyle, F.R.S., for help in the development of the idea of following the experience of successive census units, and to Mr. C. H. Wickens, Commonwealth Statistician at that time. It may also be noted that Wickens had treated deaf-mutism as recorded in the censuses of 1911 and 1921 on a generation basis in his report [18] on the 1921 census of Australia and that he was familiar with the idea of the "fluent" life table of Knibbs,[12] his predecessor. Wickens [19] speaks of "generation life tables" and it seems probable that he had intended the extensive data, collected for his 1881–1890 and 1891–1900 life tables, to be used also for the construction of generation life tables. If we are interested in past time, the methods of the "fluent" life tables of Knibbs,[13] the "census units" of Cherry,[16] the "consecutive" mortality of Davidson and Reid,[12] the "generation" of Andvord,[4] and the "cohorts" of Frost [5] may be considered as identical in theory and, perhaps, only differing in techniques of graduation. The statements of Wolfenden [20] are in general accord with this identification of the methods.

In the early years of this century it became apparent to the actuaries that death-rates were no longer constant as they had been, say, in Farr's earlier years at the office of the Registrar-General. A dissatisfaction arose with the idea that present experience could be equated with the experience of a generation. Explicit solutions were given by Knibbs,[13] M'Kendrick,[21] Derrick,[11] and Davidson and Reid.[12] In medical circles, on the other hand, there has long been a feeling that one should follow a group of persons through life rather than deduce such an experience from an existent population.[4–8 15 16] The first practical method of obtaining this biologically desirable experience of a generation or cohort was given by Cherry.[16]

School of Public Health and Tropical Medicine, University of Sydney. H. O. LANCASTER.

p-AMINOSALICYLIC ACID IN THE TREATMENT OF THROMBOPHLEBITIS

SIR,—Both cortisone [22] and phenylbutazone [23] have been given with success in the treatment of superficial thrombophlebitis, and since *p*-aminosalicylic acid possesses a cortisone-like action (presumably by virtue of its "salicylic-acid" moiety) including, also like cortisone,[24] an antithyroid action,[25] it seemed possible that this drug might also be of value in thrombophlebitis.

Accordingly 15 patients with superficial thrombophlebitis, who had no signs or symptoms of myxœdema, were treated with an increasing oral dose of *p*-aminosalicylic acid. When the dose had reached 1·5–2 g. four times daily, the severity of the pain, tenderness, and œdema diminished rapidly in all 15 cases. No controls are available, but 4 patients relapsed when the drug was withdrawn early and responded once more on its resumption. Moreover in 4 patients with chronic varicose ulcer and associated thrombophlebitis, the healing-rate increased, apparently significantly, with this treatment, concurrently with the expected improvement in their thrombophlebitis.

Dundee. J. C. ANNAND.

A CASE OF MISTAKEN IDENTITY

SIR,—Much confusion has been caused by the fact that my name is so similar to that of Dr. Geoffrey (H.) Bourne of the London Hospital. I would be grateful if you would publish this letter. I have nothing to do with ageing, except in so far as my own metabolic processes are concerned, nor have I any interest in hair growing, beards, or other such appurtenances of senility.

London, N.W.1. GEOFFREY BOURNE.

Personal Papers

MATRIARCHY

MUCH has been written about the doctor-patient relationship; but, when one becomes an inpatient, the emphasis changes at once to the relationship with nurses. It is through this that the patient is related to the life of the hospital.

* * *

Our Western society is predominantly patriarchal, in contrast to some small societies in the Pacific, where goods are inherited through the female line, work is organised by the female head of the family, and physical conflict is a crime. As I lay in my hospital bed one morning, I suddenly realised that I was in the hands of a matriarchal subsociety. The more I thought of it, the more the idea seemed to explain conundrums which surrounded me. For instance, how is it that these nursing jobs, with low pay, long hours of work, a grinding and prolonged apprenticeship, and onerous sustained responsibility succeed in attracting an endless stream of girls who are not only intelligent but above the norm of society by way of appearance? Is this a sort of female revolt? Is the lure of a fe ale-dominated society—offering escape from paternalistic influence with its insistence on the inevitable superiority of the male—such an attraction to a section of young womanhood that it causes them to ignore the superficial economic shortcomings of the profession and embrace it for its real values? Nowhere else perhaps does the female establish such an ascendancy over the male as in the nurse-patient relationship.

Whether or not this is a reason why girls take up nursing, the existence of the matriarchy itself can scarcely be questioned. Observe its serried ranks of women carefully subdivided into rigid castes, each with its distinctive uniform and badge of office so that none may unwittingly invade the privileges of another. As a manager in normal life, I envy the respect and awe given in this matriarchy to those with managerial or administrative responsibility. Sisters and matrons in hospitals seem to carry a much more pronounced aura of authority than foremen and managers in industry.

I have heard criticisms of the rigour of the discipline inflicted on nurses; but my stay in hospital makes me wonder whether any other form of training could fit females for the vigorously dominant rôle of nurse, or enable them to create that "We have the solution to all problems: please do not worry" atmosphere which nursing seems to require.

* * *

16. Cherry, T. *Med. J. Aust.* 1925, i, 581.
17. Coghlan, T. A. Transactions of the 6th Session of the Intercolonial Medical Congress of Australasia, 1902, p. 63.
18. Wickens, C. H. Statistician's Report, Census of the Commonwealth of Australia, 1921. Melbourne, 1927.
19. Wickens, C. H. *J. Inst. Actuar.* 1930, **61**, 165.
20. Wolfenden, H. H. Population Statistics and Their Compilation. Chicago, 1954.
21. M'Kendrick, A. G. *Proc. Edin. math. Soc.* 1926, **44**, 98.
22. Flickenger, F. M., Henderson, I. W. D. *Surg. Gynec. Obstet.* 1956, **102**, 66.
23. Stein, I. D. *Circulation*, 1955, **12**, 833.
24. Hill, S. R., Reiss, R. S., Forsham, P. H., Thorn, G. W. *J. clin. Endocrin.* 1950, **10**, 1375.
25. Dixon, W. M. *Brit. J. Tuberc.* 1954, **48**, 102.

The new patient when he first enters hospital is probably unaware that he is dealing with anything fundamentally different from that which exists in his home, at the club, or in the factory. He does not know what he has walked into, and that it will bamboozle him as it bamboozled me; for kindness and tolerance is the substratum on which the system is built; and this is the unexpected feature of the situation.

Immediately after his arrival in hospital his own complete lack of responsibility is quickly established in the patient's mind by such adroit manœuvres as immediately consigning him to bed, taking his temperature, and communicating a formidable list of things which he may not do. Accustomed as he is to the ways of a male-dominated society, he is now on guard against the petty persecution which is the inevitable concomitant of such a position. The events which follow stand his values on their heads. He is treated from that moment onwards with consistent authoritarian kindness of the greatest warmth. Although he, the patient, is at this stage often still able-bodied and hearty, he is cosseted, baths are run for him, lights are adjusted, pillows smoothed, concern expressed, curtains drawn. He may have become a mere object, but an impersonal warmth and kindness is the pervading atmosphere. This will continue to be the atmosphere, subject to his playing the rôle of patient consistently. At least, I think that to be so, for I played consistently and the kindness continued: it warmed my heart. If I had failed to do so I might have regretted it, but I had not the courage to experiment. Challenge a nurse and you may well find the front-rank representative of a formidable matriarchy with the glint of battle in her eyes and a range of techniques which you cannot start to match.

* * *

I do not know if what I have said sounds critical. It is not meant to be critical. It is just meant to be straight reaction.

I used to feel sorry for underpaid overworked nurses, and I still think both adjectives fit. But there are clearly aspects of this job which mean more to them than hours of work and pay, and in this respect they are extremely fortunate.

Obituary

ARTHUR JOHN JEX-BLAKE

M.A., D.M. Oxfd, F.R.C.P.

Dr. A. J. Jex-Blake, who died in Nairobi on Aug. 16 at the age of 84, had lived in Kenya for over thirty years. Earlier, while on the staff of St. George's Hospital, he had become well known in London as a consultant and teacher.

Arthur John Jex-Blake came of a talented family, one member of which, his aunt Sophia Louisa Jex-Blake, was a pioneer medical woman. He was educated at Eton and Magdalen College, Oxford, where he was a demy and took a first-class in natural science in 1896. He entered St. George's Hospital as a University scholar in 1898, and qualified B.M. three years later. In 1902 he was awarded a Radcliffe travelling fellowship by Oxford University, and this enabled him to visit centres in Denmark, Austria, and the U.S.A.

In the years that followed he was appointed first to the staff of the Victoria Hospital for Children, Chelsea, and subsequently to the staffs of the Brompton Hospital and of St. George's Hospital. He was elected F.R.C.P. in 1912, and the following year he was the college's Goulstonian lecturer, taking as his subject Death by Electric Currents and by Lightning. He was associated with five editions of *Gray's Anatomy* between 1909 and 1920, and he was himself the author of *Tuberculosis: its Forms, Treatment and Prevention* (1915) and *Physical Signs in the Chest and Abdomen* (1921).

In the 1914–18 war he served in the R.A.M.C., with the rank of major.

R. R. J., who entered St. George's Hospital in 1899, a year after Dr. Jex-Blake, writes:

I was clinical clerk to him as house-physician in 1903. His knowledge of medicine was immense and his classical scholarship prodigious, and he took lots of trouble with us. Even in his notes on outpatients he would indulge in his taste for Latin prose. Many a child's notes would begin *mater stulta*, and in moments of extreme exasperation he would add *stultissima* to the *stulta* already penned. His Oxford years had given him profound admiration for Sir William Osler, who often dropped in at St. George's to see him.

C. F., who was a clinical clerk when Dr. Jex-Blake was medical registrar at St. George's, writes:

I owed much to his insistence on extreme accuracy in recording a patient's history, symptoms, and physical signs. Later, as an outpatient physician, he concentrated on minor maladies, and his dicta on the treatment of threadworm in a child are unforgettable. Addressing the mother he said: "Ma'am, carry out the treatment I have ordered and see that the child wears cotton gloves and cotton drawers day and night. As to her clothes what you can't boil, bake and what you can't bake, burn." As a classical scholar he was at times inclined to use terms difficult to understand by the uninitiated: on one occasion he referred a patient to his corresponding outpatient surgeon with the request: "please examine this man's podex." The O.P. surgeon, not having had the benefit of a classical education, replied "Don't know where the podex is," to Jex's great joy. When he returned to England in 1919 he was clearly unable to settle down, and not very long afterwards he decided to go to Kenya where he achieved a great reputation as a physician. His departure was a loss to St. George's as his personal popularity, his methods of teaching, and his meticulous care for his patients would have been a great asset to the post-war generation of students.

Dr. Jex-Blake's wife died in 1951. He is survived by a daughter.

ERIC ARNOLD SCOTT

M.R.C.S., F.F.A. R.C.S., D.A.

Dr. Eric Scott, physician-superintendent and anæsthetist to Orpington Hospital and consultant anæsthetist emeritus to Guy's Hospital, died on Aug. 11. After qualifying from University College Hospital in 1915, he served in the R.A.M.C., and in 1919 he began his long association with Guy's Hospital. He was appointed anæsthetist to the hospital and to the dental school. In September, 1939, he went to Orpington Hospital, to which a large part of Guy's was transferred, as consultant anæsthetist and deputy medical superintendent, and in 1945 he became superintendent.

A. T. F. writes:

The older generation of Guy's men will remember "Tubby" Scott as one of the honorary anæsthetists who, up to the outbreak of the late war, was a familiar figure at the hospital. The apparent ease with which he gave a difficult anæsthetic concealed the skill which lay behind his work.

The early days of the war were strenuous in producing order out of the chaos which was inevitable in moving a large number of patients, staff, and students from Guy's to Orpington. Scott took up his residence in the hospital and played a very large part in organising the new service. When the air-raids started in the autumn of 1940 he made a practice of doing a ward round at night, visiting every ward during or after a raid, and he was a very great help in keeping up the morale of the patients and everyone else at the hospital.

The younger generation will remember him as a genial figure with a great sense of humour, who was always ready to help them at what was often a difficult time in their career, while his short-lived flashes of anger made easy his comparison to Mr. Pickwick. At the end of the war he became medical superintendent and guided the hospital through the difficult transition stages, firstly when the Emergency Medical Service was merged in the National Health Service, and later when Guy's staff and nurses returned to Guy's, and Orpington came to stand on its own feet as a general hospital, with its own nurses' training-school.

During the latter years of his life his health was not good, but up to his final illness he remained in charge of the hospital, and he will be very sadly missed both by the practitioners outside the hospital and by all the hospital staff.

Notes and News

CHARING CROSS HOSPITAL

THE board of governors of Charing Cross Hospital has accepted in principle a proposal by the Ministry of Health for the rebuilding of the hospital and the associated medical school on the site of Fulham Hospital in West London. The Ministry's proposal has been approved by the University Grants Committee and the University of London. The former plan, which called for reconstruction of hospital and school at Northwick Park, was opposed by the U.G.C. and the university on the score that this site was too far from the centre of London.

A DANISH CENTENARY

ON Sept. 1 the centenary of the Danish Medical Association is to be celebrated in Copenhagen. The Almindelige Danske Lægeforening was founded on Sept. 1, 1857, by Dr. Andreas Black (1819–1892); and its membership has swelled from an initial 80 to 1500 in 1907 and 5689 at the present time. The association's fine house in Copenhagen, Domus Medica, was bought in 1948 to replace the old Domus Medica, near Amalienborg Castle, which was blown up in the 1939–45 war as a reprisal against Danish doctors who opposed the German occupying force. The chairman this year is Dr. Charles Jacobsen, a general practitioner in Copenhagen.

SURGEONS' BATTLE

A NEW popular history of medicine,[1] written by an American lay writer, is essentially a history of surgery describing in biographical form those who have fought the four great battles for the control of hæmorrhage, pain, infection, and shock. These accounts include Vesalius, Paré, Harvey, John Hunter, Ephraim McDowell, Lister, Halsted, and Cushing. They are well written, but medical detail is scanty, and there are curious twists of emphasis. The account of Hunter stresses the eccentric and ludicrous sides of his character, until the author sees for the first time Reynolds's portrait in the Royal College of Surgeons; she then realises that he was "beyond everything else an idealist, a visionary, a poet of science." The macabre, bizarre background of Paris in the days of Vesalius and his constant quarrels with Sylvius dominate this section of the book.

LEFT-HANDED DOCTOR

READERS whose memories reach back to our preperipatetic Grains and Scruples series will recall the lively and free-ranging pen of Peter Quince, bellows-mender. In a new book[2] the same pen, candid almost to embarrassment, tells the story of his seven years in a Norfolk village practice, before bellows-mending claimed him for its own. Granting always that our profession's prevailing practice or pastime of undressing in public almost to nakedness is a good one, the book can be warmly commended.

A left-handed doctor is, in this case, one who conducts village operatic and choral societies with his right hand, his practice with his left—or so Peter Q. would have us believe. Each hand, it seems, after some initial gaffes, learned and did its job, and even worked in, more or less, with the other, giving, each in its field, some very creditable performances. The book should prove instructive to the larval doctor, revealing to the layman, and entertaining to both.

University of Cambridge

On Aug. 3, the following degrees were conferred:

M.D.—T. B. Anderson, *G. H. Dhenin, R. L. Huckstep, J. S. Mitchell, M. J. D. Newman, J. R. H. Pinkerton, C. B. Prowse, T. J. Rendle-Short, R. V. Walley, Pow-Meng Yap.

M.B. B.Chir.—*R. A. Barron, N. G. A. Gracey, J. G. Halberstam, A. J. Hosking, *J. E. Portelly, *T. S. Worthy.

M.B.—*Rahul Banerjee, P. A. F. Chalk, W. J. Cliff, *D. A. Crockford, *T. R. P. Cullinan, *Katharine E. Cuthbert, Sonia R. Dias Bandaranaike, *D. C. Dumonde, *M. W. Haslett, I. M. Jessiman, *B. A. Latham, D. A. Nightingale, *J. W. B. Palmer, Anne W. Perver, R. A. N. Petrie, *D. W. Potts, *J. E. Robinson, *June M. Wilby, *Elma P. Wyatt.

* By proxy.

1. Scalpel: Men Who Made Surgery. By AGATHA YOUNG. London: Robert Hale. 1957. Pp. 311. 21*s*.
2. Left Handed Doctor. By PETER QUINCE. London: J. M. Dent. 1957. Pp. 194. 16*s*.

University of Oxford

At a congregation on Aug. 3 the degree of B.M. was conferred on the following:

Mary M. Addison, S. R. Coverley, Ruth S. Davies, and A. J. Ferris.

University of London

The following degrees have been awarded:

M.D.—K. R. Dempster, Stanley Dische, A. E. Dormer.
M.S.—Marco Caine, J. C. S. Leverton.

College of General Practitioners

The first Pfizer lecture of the Northern Home Counties Faculty of the college will be delivered on Sept. 26 at University College Hospital Medical School, London, W.C.1, at 8 P.M., by Lady Isobel Barnett, M.B., whose subject will be Why Don't we Live to be a Hundred?

The lecture is open to doctors who are not members of the college. Tickets may be had from Dr. D. G. Wilson, 19, Chiltern Avenue, Bushey, Herts.

Radio-isotopes in Scientific Research

An international conference on radio-isotopes in scientific research, convened by UNESCO, will be held in Paris on Sept. 9–20. Sir John Cockcroft, director of the Atomic Energy Research Establishment, will preside over the conference. The main purpose of the conference will be the exposition and discussion of new ideas and methods for the use of radio-isotopes in biology, physiology, agriculture, medicine, oceanography, and industrial research. Further information can be had from UNESCO House, 19, Avenue Kléber, Paris, 16.

Ophthalmological Society of the United Kingdom

This society offers a Treacher Collins prize (£100) for the best essay, by a doctor of any nationality, on the Eye in Relation to the Collagen Diseases. Essays should be submitted by Dec. 31, 1959, to the hon. secretary of the society, 45, Lincoln's Inn Fields, London, W.C.2.

CORRIGENDUM: *Surgery in Hæmophilia.*—In the article by Dr. R. G. Macfarlane and his colleagues (Aug. 10, p. 251) the reference to Fraenkel, G. J. (1957) should have read *J. R. Coll. Surg. Edinb.* (in the press).

Appointments

COOPER, R. S., M.B. Lond., D.P.H.: deputy M.O.H., deputy principal M.O., Luton.

DISLEY, PHYLLIS J., M.B. Glasg., D.P.H.: assistant M.O., public health department, Liverpool.

ELITHORN, ALICK, M.D. Camb., M.R.C.P.: part-time consultant physician in psychological medicine, Royal Free Hospital Group, London.

HUNT, F. T., M.B. Lond., D.P.H.: senior assistant M.O.H., Derby.

JONES, BRYAN, M.B. Wales, B.SC.: M.O., North Western Gas Board, Manchester.

MUCKLOW, E. H., M.B. Birm., D.M.R.D., F.F.R.: consultant radiologist, United Birmingham Hospitals.

POOL, MONICA B., M.B. Sheff., D.C.H.: assistant M.O.H., assistant school M.O., Oldham.

REEVES, R. G. W., M.B. Birm.: part-time medical superintendent, Chard and District Hospital (chronic sick section).

WILLIAMS, MARY P. K., M.B. Lpool., D.P.H.: assistant M.O., public health department, Liverpool.

Fife County Council:

FRASER, I. A., M.B. Aberd., D.P.H., D.C.H.: assistant M.O., Cowdenbeath area.

GARDINER, ROBERT, M.B. Aberd., D.P.H.: assistant M.O., Auchterderran area.

INNES, GEORGE, M.B. Aberd., D.P.H.: assistant M.O., Markinch area.

Sheffield Regional Hospital Board:

JOHNSTONE, J. M., M.D. St. And.: consultant pathologist-in-charge, Grimsby area hospitals.

KIDD, H. B., M.B. Camb.: senior assistant psychiatrist, Carlton Hayes hospital, Narborough, nr. Leicester.

MACFARLANE, ARCHIBALD, M.B. Edin., M.R.C.P.E.: consultant pathologist, Mansfield area hospitals.

Births, Marriages, and Deaths

BIRTHS

CARTER.—On Aug. 18, at Redhill County Hospital, to June (née Jarvis) and Keith Carter—a daughter (Valerie Jill).

DICKINSON.—On Aug. 15, at University College Hospital, London, to Elizabeth (née Farrell) and John Dickinson—a daughter.

LICHTER.—On June 29, in Johannesburg, to Heather (née Lloyd) and Ivan—a daughter, Shelley, sister to David, Jonathan, and Barry.

The pathway of infection is broad and open

Inevitably, someone succumbs. When the symptoms of bacillary dysentery become evident, 'Thalazole' is indicated for immediate administration. The effect of this is dramatic. Within a few hours griping ceases and diarrhoea is markedly reduced. Rapid convalescence may be anticipated.

Detailed literature is available on request

INDICATIONS

BACILLARY DYSENTERY
TREATMENT OF THE CARRIER STATE
PRE- AND POST-OPERATIVE USE IN INTESTINAL SURGERY

SUPPLIES

Tablets of 0·5 gramme and a **suspension** containing 0·75 gramme per fluid drachm (3·6 c.c.).

'THALAZOLE'
trade mark brand
PHTHALYLSULPHATHIAZOLE

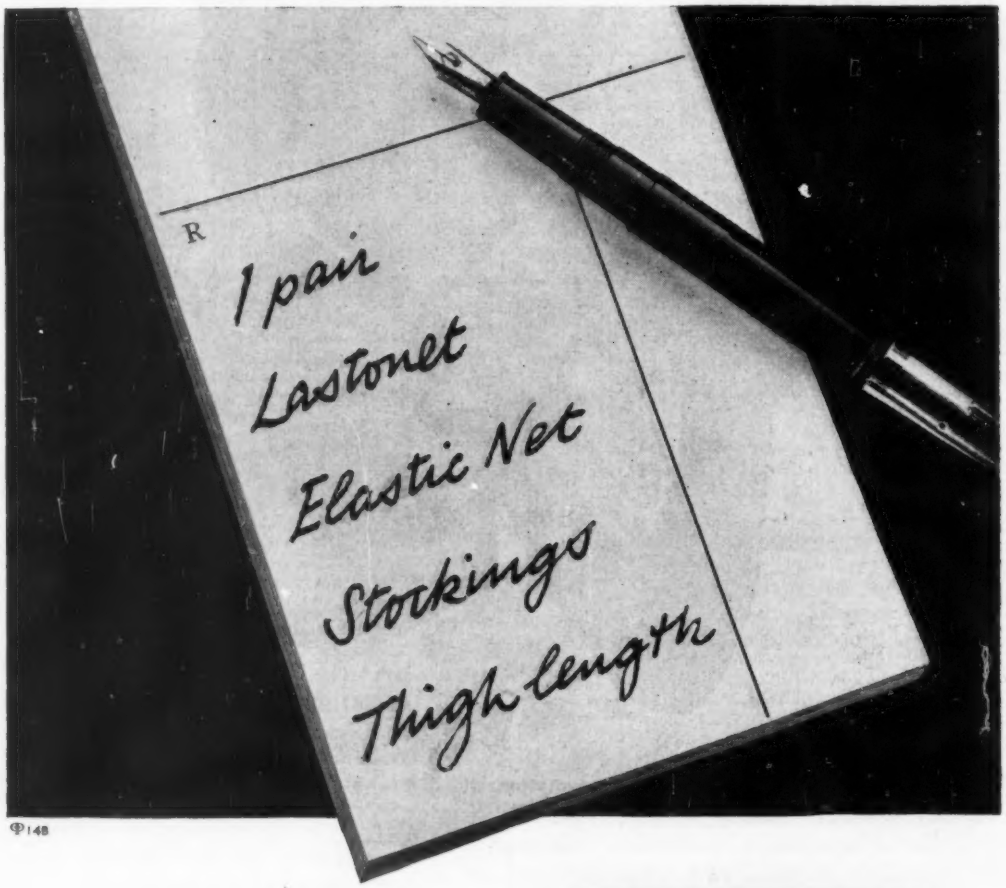
MANUFACTURED BY
MAY & BAKER LTD

An **M&B** *brand Medical Product*

MA454B

DISTRIBUTORS
PHARMACEUTICAL SPECIALITIES (MAY & BAKER) LTD · DAGENHAM

"I'm going to prescribe Lastonet stockings"



Φ148

And this is how to do it. The words "ELASTIC NET STOCKINGS" *must* be written on the E.C.10 to obtain Lastonet stockings for supply under the National Health Service. The quantity required and whether thigh or knee length should also be included. The correct wording is important to ensure Lastonet stockings which are made only to *individual* measures and so ensure a perfect fit.

Lastonet
ELASTIC
NET STOCKINGS

IN **NYLON** OR COTTON

LASTONET PRODUCTS LIMITED,
CARN BREA, REDRUTH, CORNWALL

STANDS ALONE IN DERMATOLOGICAL PRACTICE

The active principle in
WRIGHT'S COAL TAR SOAP

A UNIQUE APPLICATION FOR THE SKIN

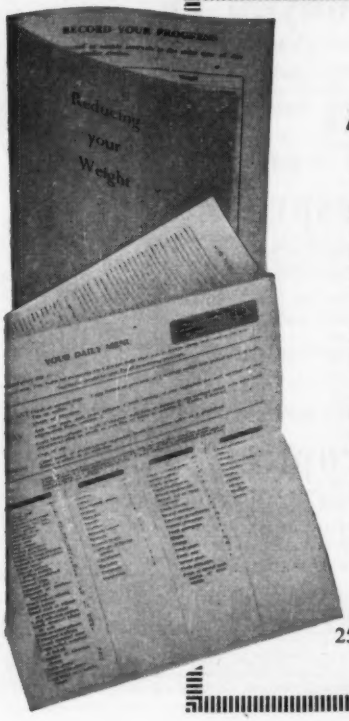
—the original solution abstracting the unique antiseptic and healing virtues of coal tar

Today, over 90 years since its discovery by the founder of the house of Wright's, it is still to the fore in dermatological practice. Uniform and stable in composition, and with remarkable antipruritic and stimulating properties, it is particularly indicated for many kinds of scaly or parasitic skin diseases.

Wright's
LIQUOR CARBONIS DETERGENS

Continuous research in germicides ensures constant improvement to meet all modern dermatological requirements.

WRIGHT LAYMAN & UMNEY LTD., 42/50 SOUTHWARK STREET, LONDON, S.E.1



SUPPLIES OF THIS FOLDER ARE AVAILABLE FREE OF CHARGE

"Reducing Your Weight" is a new and easily followed guide to diet for weight reduction, and includes some simple advice and a varied menu. The folder is designed for handing to the patient, whose name may be written in a space provided on the cover.

Quantities of this folder are available free of charge to medical practitioners. For a supply, or a specimen copy, write to the Energen Dietary Service at the address below.

The Energen Dietary Service, staffed by qualified dietitians and under medical supervision, offers information and practical assistance in all dietary and nutritional problems. All services are free of charge, and practitioners are invited to apply for details.

Available in the U.K. only.

The Secretary
ENERGEN DIETARY SERVICE
25a, Bryanstone Square, London, W.1. Tel: AMBassador 9332

ASTHMA

Rely on Rybar for Instant Relief

Ever increasing numbers of medical men are relying on Rybarvin Inhalant to combat bronchospasm. The Ministry of Health having agreed to the prices of Rybar asthma inhalants, Rybarvin can be freely prescribed.

RYBARVIN brings relief. Consistently, often spectacularly, attacks are cut short and their frequency lessened. Free from excess acid, non-irritant and non-habit-forming, it is an ideal inhalant for all asthmatics, young and old.

Formula

Pituitary Extract. Posterior and Anterior Lobe	0·40% w/v
Methylatropine Nitrate	0·14% w/v
Papaverine	0·08% w/v
Adrenaline	0·40% w/v
Ethyl Para-aminobenzoate	0·20% w/v
Iso-butyl Para-aminobenzoate	0·01% w/v

RYBAR INHALER has been specially designed for aerosol therapy. Both Rybarvin and the Inhaler may be prescribed in N.H.S. Form E.C.10.

Samples and details of trial outfits forwarded on request.

TANKERTON **RYBAR** KENT
LABORATORIES LTD.
P.B25

WHEN PRESCRIBING CHLORODYNE
medical men should be particular to specify

Dr. J. Collis Browne's CHLORODYNE

The Original and only genuine Chlorodyne

used with unvarying success by the Medical Profession in all parts of the world for over **100 YEARS**

Always insist on "Dr. Collis Browne's"

THERE IS NO SUBSTITUTE

The
MERCK SHARP & DOHME

'Hydro' Quartet

Hydrocortisone preparations for the treatment of lesions of the SKIN, JOINTS, NOSE AND EYES

OINTMENT
'Hydroderm'
'HYDROCORTONE'-NEOMYCIN-BACITRACIN
For inflammatory conditions of the skin, especially when infection is present. ***Tubes of 5 G. and 15 G.***

TABLETS
'Hydrodyne'
'HYDROCORTONE'-ASPIRIN
Anti-inflammatory, anti-rheumatic, analgesic therapy for rheumatic and allied diseases. ***Bottles of 100.***

NASAL SPRAY
'Hydrospray'
'HYDROCORTONE'-'PROPADRIN'-NEOMYCIN
Safe nasal therapy for hay fever, rhinitis, polyposis and similar allergic conditions.
Spray bottles of 15 ml.

EYE DROPS
'Hydroptic'
'HYDROCORTONE'-NEOMYCIN
For inflammatory lesions of the eye, especially when infection is present.
Plastic applicator of 5 ml.

Fuller details on application

MSD **MERCK SHARP & DOHME LIMITED, HODDESDON, HERTS.**

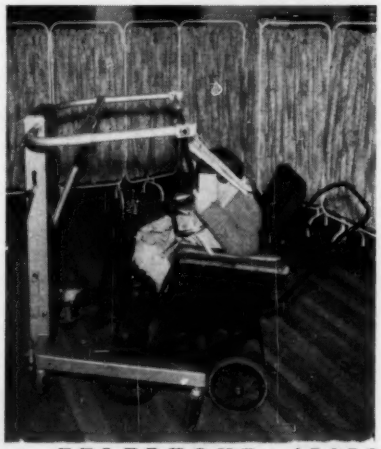
Product names in inverted commas are Trade Marks

Above: This illustrates the horizontal hoist with patient ready for transit.

The 'Little Plumstead' PATIENT LIFTER

A NEW MULTI-PURPOSE HOIST REQUIRING ABSOLUTELY NO EFFORT OR CO-OPERATION FROM THE PATIENT

Right: The vertical hoist, used to lower patient into wheel-chair.



Extremely heavy and helpless patients can be easily and safely lifted with this ingenious hydraulic hoist. Simple to operate, the apparatus is available with two quickly interchangeable heads, which lock into the main frame. The horizontal head allows helpless bed patients to be moved between departments without fuss or strain, either to the patient or nursing staff. In cases where it is necessary to move patients from chair to bed, lavatory seat or bath the verticle head ideally solves the problem. As an extra, a weighing device is incorporated into the hoist, an essential item for nursing staff dealing with helpless cases. Interchangeable heads are available separately.

For descriptive literature please write to:

MANN EGERTON & CO. LTD

MANUFACTURING ENGINEERS

CROMER ROAD WORKS : NORWICH : TELEPHONE: 47272

BARBEVITE ELIXIR

FOR NEURASTHENIA AND ANXIETY STATES

This pleasantly flavoured elixir contains Phenobarbitone together with Vitamins B_1, B_2, B_6 and Nicotinamide. Ideally suited for the treatment of various conditions associated with the B complex deficiencies such as general fatigue, anorexia, gastro-intestinal disturbances, tachycardia, irritability and depression.

FORMULA.

Phenobarbitone B.P. ¼ grain. Aneurin Hydrochloride B.P. 1.5 mgm. Riboflavine B.P. 1.0 mgm. Pyridoxine Hydrochloride B.P.C. 0.17 mgm. Nicotinamide B.P. 10. mgm. Glycerin B.P. 42 minims. Alcohol B.P. 9 minims. Colour and flavour a sufficiency. Base to 1 fluid drachm.

POISON | S1 | S4

PRESENTATION.

In screw-capped bottles. 5 fl. ozs. 5/10: 20 fl. ozs. 21/8: 80 fl. ozs. 76/10. Subject to professional discount. Dispensing packs exempt from purchase tax. Samples available on request.

Manufactured in the laboratories of

JAMES WOOLLEY, SONS & CO. LTD., VICTORIA BRIDGE - MANCHESTER 3.

WBI

From milk to mixed diet

HOW HEINZ STRAINED FOODS HELP

Mothers of three or four-month-old babies often need your practical advice about how to start baby on a mixed diet.

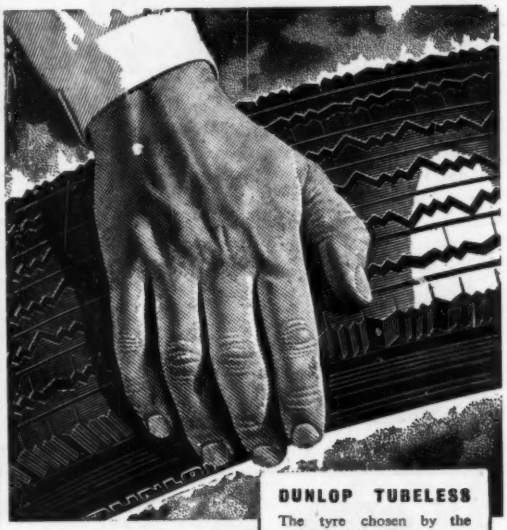
When you suggest Heinz Strained Foods you can do so with complete confidence. The 19 different foods, introduced gradually from about three-months onwards, between them offer scope for a varied diet. They are cooked and strained under strictly controlled conditions, with the minimum loss of food values. And, of course, they are prepared much more hygienically than they would be in an ordinary kitchen.

For full details of the nutrient values of the 19 varieties of Heinz Strained Foods, write to Dept. T2, H. J. Heinz Co. Ltd., Harlesden, London N.W.10.

HEINZ 57
Strained Foods

MEAT BROTHS · SOUPS · VEGETABLES · SWEETS · CEREAL

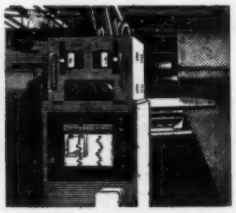
They build durability at Fort Dunlop



DUNLOP TUBELESS
The tyre chosen by the majority of British car manufacturers to give you *more confident motoring.*

with Science, Accuracy and Experience

More miles: extra toughness; longer life and complete reliability—that's what they build into tyres at Fort Dunlop. The scientists, the engineers and the men on the production line are all experts because tyre building is an expert's business, and they know more about tyre building at Fort Dunlop than anywhere else in the world.



Atoms for accuracy. *Atomic radiation operates this Beta Ray Gauge, which maintains a continuous check on rubber thickness and reveals the smallest deviation from specification. The thickness covering each layer of cord must be absolutely uniform and accurate within minute tolerances to produce true durability.*

DUNLOP

built better to last longer!

714/123

GENERAL AND CARDIAC SEDATIVE

NATISEDINE

Tablets 0.1 gm. Phenylethylbarbiturate of Quinidine
(Bottles of 20 and dispensing packs of 100.)

INDICATIONS

Anxiety states - Insomnia - Nervousness - Distress - Palpitation - Premature beats
Cases resistant to other sedatives.

LABORATORY NATIVELLE Ltd.
74-77 White Lion Street, LONDON, N.1 18-19 Temple Bar, DUBLIN

For the treatment of

VARICOSE ULCERATION

"CELLANBAND"
THE ORIGINAL
MODIFIED UNNA'S PASTE BANDAGE
and
"Peraban"
THE ORIGINAL
DIACHYLON CREPE ADHESIVE BANDAGE
Both these effective and old-established bandages are
AVAILABLE ON E.C.10
Please send for Literature
Cuxson, Gerrard & Co. Ltd. OLDBURY, B'HAM
'Phone: BROadwell 1355

NAPT
MEMORIES
Sir Robert W. Philip 1857-1939
OF HIS FRIENDS AND PUPILS
Physician and medical statesman, pioneer against tuberculosis, and a personality whom no patient, friend, or pupil will ever forget.
"*This remarkable little collection of vignettes*".
Scotsman.
96 pages, including illustrations and appendices. 12/6
Order direct from **NATIONAL ASSOCIATION FOR THE PREVENTION OF TUBERCULOSIS,** Tavistock House North, Tavistock Square, London, W.C.1, or from 65, Castle Street, Edinburgh, 2.

BOWDEN HOUSE
HARROW-ON-THE-HILL, MIDDLESEX
Established in 1911 Tel.: BYRon 1011 & 4772
(Incorporated Association not carried on for profit)
A private clinic for the treatment of the neuroses and nervous disorders by psychotherapy and all modern physical therapies.
Apply: MEDICAL DIRECTOR

SPRINGFIELD HOUSE
Phone: BEDFORD 3417 **Near BEDFORD**
For MENTAL CASES (including the aged)
Fees from Ten Guineas per week
For forms of admission, &c., apply to the Resident Physician CEDRIC W. BOWER.
INTERVIEWS IN LONDON BY APPOINTMENT.

CLIFFDEN, TEIGNMOUTH

For the early treatment of nervous disorders and patients needing rest and care

A well-appointed House with spacious balconies and extensive views of the South Devon Coast. Beautiful garden and own dairy in 35 acres In the same grounds, **ROWDENS,** a comfortable house with lovely views. Private road to the beach
There is also a charming house, **EBWORTHY, MANATON, DARTMOOR,** situated in 25 acres, 1100 ft. up for bracing moorland air
Resident Physicians—BERTHA M. MULES, M.D., B.S. ANNE S. MULES, M.R.C.S., L.R.C.P. *Telephones*—TEIGNMOUTH 289 and 537

RUTHIN CASTLE, NORTH WALES
A Private Clinic, the first in Great Britain, for investigation and treatment of all forms of disease, except infectious and mental
Nursing, dietetic, massage, x-ray and laboratory departments **Central heating and a lift to all floors**
Inclusive charges Apply SECRETARY Telephone: Ruthin 66

ST. ANDREW'S HOSPITAL FOR NERVOUS AND MENTAL DISORDERS
NORTHAMPTON

PRESIDENT: THE EARL SPENCER

MEDICAL SUPERINTENDENT: THOMAS TENNENT, M.D., F.R.C.P., D.P.H., D.P.M.

This Registered Hospital is situated in 130 acres of park and pleasure grounds. Voluntary patients, who are suffering from incipient mental disorders or who wish to prevent recurrent attacks of mental trouble; temporary patients, and certified patients of both sexes are received for treatment. Careful clinical, biochemical, bacteriological, and pathological examinations. Private rooms with special nurses, male or female, in the Hospital or in one of the numerous villas in the grounds of the various branches can be provided.

WANTAGE HOUSE

This is a Reception Hospital in detached grounds with a separate entrance, to which patients can be admitted. It is equipped with all the apparatus for the complete investigation and treatment of Mental and Nervous Disorders by the most modern methods; insulin treatment is available for suitable cases. There is an Operating Theatre, a Dental Surgery, an X-ray Room, an Ultraviolet Apparatus, and a Department for Diathermy and High-frequency treatment. It also contains Laboratories for biochemical, bacteriological, and pathological research. Psychotherapeutic treatment is employed when indicated.

MOULTON PARK

Two miles from the Main Hospital there are several branch establishments and villas situated in a park and farm of 650 acres. Milk, meat, fruit, and vegetables are supplied to the Hospital from the farm, gardens, and orchards of Moulton Park. Occupational therapy is a feature of this branch, and patients are given every facility for occupying themselves in farming, gardening, and fruit growing.

BRYN-Y-NEUADD HALL

The seaside house of St. Andrew's Hospital is beautifully situated in a park of 330 acres, at Llanfairfechan, amidst the finest scenery in North Wales. On the North-West side of the Estate a mile of sea coast forms the boundary. Patients may visit this branch for a short seaside change or for longer periods. The Hospital has its own private bathing house on the seashore. There is trout-fishing in the park.

At all the branches of the Hospital there are cricket grounds, football and hockey grounds, lawn tennis courts (grass and hard courts), croquet grounds, golf courses, and bowling greens. Ladies and gentlemen have their own gardens, and facilities are provided for handicrafts, such as carpentry, etc.

For terms and further particulars apply to the Medical Superintendent (TELEPHONE: Northampton 4354 (3 lines)), who can be seen in London by appointment.

HEIGHAM HALL, NORWICH

PRIVATE MENTAL HOME for Nervous and Mental illness. All types of treatment carried out. Accommodation for Alcoholics and Addicts available. Special Geriatric Unit now open. Fees from 7 gns. per week upwards according to requirements.

Apply to Dr. J. A. SMALL Telephone: Norwich 20080

WYKE HOUSE HOSPITAL
ISLEWORTH, MIDDLESEX

Telephone: EALing 7000

A private home for the individual treatment of all forms of nervous and mental illness, including alcoholism.

H. PULLAR-STRECKER, M.D. G. W. SMITH, O.B.E., M.B., CH.B.

CHISWICK HOUSE
PINNER, MIDDLESEX

Telephone: PINNER 234

A private Nursing Home for patients suffering from all forms of Nervous and Psychological illness. Forty-four patients of both sexes. A certain number of elderly patients received. All modern forms of treatment. Psychotherapy, Electroplexy, Modified Insulin, etc. Two country houses in adjoining grounds of 5 and 6 acres each respectively, 12 miles north-west of London. Frequent trains Baker Street Station to Pinner. One-quarter of a mile from Pinner Station.

Apply to the Medical Director, DOUGLAS MACAULAY, M.D., D.P.M.

THE MEDICAL PROTECTION SOCIETY LIMITED

Over 60 years experience in medical defence and protection

Complete indemnity granted to members in cases undertaken on their behalf

ANNUAL SUBSCRIPTION: £1 for first three years for newly qualified entrants and £2 thereafter

Full particulars from the Secretary (Dr. Alistair French), Victory House, Leicester Sq., W.C.2. Gerrard 4553 and 4814

Vacancies

ACADEMIC AND EDUCATIONAL SECTION — Page 34

ADMINISTRATIVE
Scotland. South-Eastern R.H.B. M.O. 43

ANÆSTHETICS
Hammersmith Hosp. & Postgraduate Med. School. Sr. Reg. 35
London, E.1. Reg. 36
National Temperance, N.W.1. Reg. 36
Birmingham. Dudley Road. Sr. H.O. 38
Broxburn. Bangour Gen. Reg. .. 38
Burton-on-Trent. Gen. Jr. H.M.O... 38
Chertsey. St. Peter's. Locum Sr. H.O. 39
Crewe & Dist. Mem. Jr. H.M.O. .. 38
Edgware Gen. Sr. Reg. 39
Kettering Gen. Sr. H.O. 40
Leeds R.H.B. P.-t. Cons. 35
Lincoln. St. George's. Reg... .. 41
Luton & Dunstable. Locum Reg. .. 40
Luton & Dunstable. Reg. 40
Manchester. South Manchester H.M.C. Sr. H.O. 41
Newcastle R.H.B. Reg. 42
Northampton Gen. H.O. 42
Northwood. Mount Vernon. Reg. .. 42
Oxford United Hosps. Regs... .. 42
Salisbury Gen. Reg. 42
Scotland. Northern R.H.B. Reg... 43
Sheffield R.H.B. P.-t. Sr. H.M.O. .. 35
Shrewsbury. Royal Salop Infy. & Copthorne. Sr. H.O. 42
South East Met. R.H.B. Regs. .. 43
U.S.A. Cambridge, Mass. Residencies 45

CARDIOLOGY
Hosp. for Sick Child., W.C.1. P.-t. M.O. 34
National Heart, W.1. Sr. H.O. or Reg. 36
National Heart (Maids Moreton, Bucks). Sr. H.O. 36

CASUALTY
Connaught, E.17. Sr. H.O. 35
Hampstead Gen., N.W.3. Sr. H.O. .. 36
Aylesbury. Royal Bucks. Locum Sr. H.O. 37
Blackpool. Victoria. Sr. H.O. .. 38
Broxburn. Bangour Gen. Sr. H.O... 38
Cardiff. St. David's. Sr. H.O. .. 38
Cardiff United Hosps. Sr. Cas. O. (Sr. H.M.O.) 34
Chesterfield Royal. H.O. or Sr. H.O. 39
Hertford County. Sr. H.O. 39
Hitchin. Lister. H.O... 40
Hull. Victoria Hosp. for Sick Child. Locum Sr. H.O. 40
Newcastle Gen. Sr. H.O. 42
Newport, Mon. Royal Gwent. Sr. H.O. 42
Reading & Dist. H.M.C. Sr. H.O. .. 42
Stockport Infy. Locum Sr. H.O... 44
Watford. Peace Mem. Sr. H.O. .. 44

CHEST AND TUBERCULOSIS
Brompton, S.W.3. H.O.'s 35
London Chest, E.2. Reg. 36
Benenden Chest Hosp. Sr. H.O. .. 37
Birmingham (Sanatoria) Group H.M.C. Jr. H.M.O. 38
Glasgow. Robroyston. Jr. H.M.O. .. 39
Halifax. Northowram Hall. Sr. H.O. 40
Hexham. Wooley San. Jr. H.M.O... 39
Leeds R.H.B. Reg. 40
Liverpool. Newsham Gen. Jr. H.M.O. or Sr. H.O. 41
Maidstone. Preston Hall. Sr. H.O... 41
Northampton. Creaton. Sr. H.O. & H.O. 42
Shotley Bridge Gen. Sr. H.O. or H.O. 43
Watford Chest Clinic. Reg... .. 44
Welsh R.H.B. Reg. 44

DERMATOLOGY
Birmingham. Skin. Sr. H.O. or H.O. 37
Leicester Royal Infy. & Gen. Hosp. Reg. 41
Scotland. North-Eastern R.H.B. Reg. or Sr. Reg. 43

EAR, NOSE, AND THROAT
Hosp. for Sick Child., W.C.1. Sr. Reg. 37
North East Met. R.H.B. Reg. .. 36
Royal Free, W.C.1. Sr. Reg. .. 36
Whittington, N.19. Locum Reg. .. 37
Ipswich & East Suffolk. H.O. .. 40
Kingston, Surrey. Sr. H.O. 40
Leeds United Hosps. Sr. H.O. .. 40

ENDOCRINOLOGY
Guy's, S.E.1. P.-t. Reg. 36

GERIATRICS
South West Met. R.H.B. Cons. .. 34
Whittington, N.19. H.O. 37
Kettering & District H.M.C. Sr. H.O. 40
West Herts Group H.M.C. Reg. .. 44

HÆMATOLOGY
Postgraduate Medical School & Hammersmith Hosp., W.12. Reg. .. 36

INFECTIOUS DISEASES
Eastern, E.9. H.O. 35
Hendon Isolation, N.W.9. Jr. H.M.O. & Locum Jr. H.M.O. 36
Neasden, N.W.10. Locum Reg. .. 36
Irvine. Ayrshire Central. Jr. H.M.O. 40
Leeds R.H.B. Reg. 40
Southampton Chest. Sr. H.O. .. 43

LARYNGOLOGY AND OTOLOGY
Hillingdon. Uxbridge. Reg... .. 39

MEDICINE
Bolingbroke, S.W.11. Locum H.O. .. 35
Lambeth, S.E.11. H.O. 36
North East Met. R.H.B. Reg. .. 36
South West Met. R.H.B. P.-t. Cons. 34
St. Stephen's, S.W.10. H.O... 37
Whittington, N.19. H.O.'s 37
Aylesbury. Stoke Mandeville. H.O... 37
Blackpool. Victoria. Pre-reg. H.O.'s 38
Brighton. Royal Sussex County. Pre-reg. H.O.'s 38
Cambridge. Addenbrooke's. Locum Reg. 38
Derby. City. Pre-reg. H.O. or Sr. H.O. 39
Dewsbury. Staincliffe Gen. Jr. H.M.O. 39
Hastings H.M.C. Locum R.M.O. .. 39
Leeds. Chapel Allerton. Sr. H.O... 40
Leeds R.H.B. Reg. 40
Lincoln. St. George's. Reg... .. 41
Manchester R.H.B. Reg. 41
Newton Abbot. Sr. H.O. 41
Oxford R.H.B. Reg... 42
Portsmouth Group H.M.C. Pre-reg. H.O. 42
Rochford, Essex. Gen. Pre-reg. H.O. 42
Scotland. Northern R.H.B. Jr. H.M.O. 43
Scotland. Western R.H.B. Regs. .. 43
Southampton. Royal South Hants. H.O. 43
Southend-on-Sea Gen. Locum Reg. 43
Stirling & Clackmannan Hosps. B.O.M. H.O. 43
Taplow. Canadian Red Cross Mem. Pre-reg. H.O. 44
West Dorset Group H.M.C. H.O.'s .. 44
Winchester. Royal Hampshire County. Pre-reg. H.O. 44
Wolverhampton. New Cross. Pre-reg. H.O. 45
Northern Ireland Hosps. Auth. Tutor/Reg. 45
South Africa. Donald Fraser Hosp. A.M.O. 45
Tasmania. Launceston Gen. Deputy Superintendent 35

NEUROSURGERY
Manchester. Crumpsall. Reg. .. 41

OBSTETRICS AND GYNÆCOLOGY
St. James', S.W.12. H.O. 37
Whittington, N.19. H.O.'s.. 37
Birmingham R.H.B. Reg. 38
Birmingham United Hosps. H.O. .. 38
Blackpool. Victoria. Pre-reg. H.O. .. 38
East Fife Hosps. B.O.M. Reg. .. 39
Edgware Gen. H.O.'s.. 39
Gateshead. Queen Elizabeth Hosp. Sr. H.O. 39
Isleworth. West Middlesex. Reg... 40
Nottingham City. Sr. H.O. or H.O. 42
Sheffield. Nether Edge. Sr. H.O. .. 43
Southampton Gen. H.O. 43
South East Met. R.H.B. Reg. .. 43
Northern Ireland Hosps. Auth. P.-t. Cons. 35

OPHTHALMOLOGY
Doncaster Royal Infy. Sr. H.O. .. 39
Leeds R.H.B. Locum Cons. or Sr. H.M.O. 35
Leeds R.H.B. Reg. 40
Liverpool United Hosps. Locum Sr. Reg. 41

ORTHOPÆDICS
Beverley, Westwood. H.O. 37
Blackpool. Victoria. Pre-reg. H.O. 38
Bolton. Royal Infy. Sr. H.O. .. 38
Caerphilly. Pre-reg. H.O. 38
Carluke, Lanarkshire. Law. H.O. .. 38
Colchester Group H.M.C. H.O. & Locum Reg. 39
Exeter. Royal Devon & Exeter. Sr. H.O. 39
Farnborough, Kent. Sr. H.O. .. 39
Ipswich & East Suffolk. H.O. .. 40
Kingston, Surrey. Locum Sr. H.O... 35
Kingston, Surrey. Locum Sr. H.M.O. 35
Manchester R.H.B. Reg. 41
Newcastle United Hosps. Reg. .. 42
Northampton Gen. H.O. 42
Nottingham Gen. Sr. H.O. 42
Oswestry. Robert Jones & Agnes Hunt Orthopædic. Sr. H.O. .. 42
Oxford United Hosps. & R.H.B. Sr. Reg. 42
Sheffield R.H.B. P.-t. Cons. 35
Welsh R.H.B. Sr. Reg. 44
Wrexham. War Mem. Sr. H.O. .. 44

PÆDIATRICS
Hosp. for Sick Child., W.C.1. Sr. H.O. 37
Westminster Child's, S.W.1. Sr. Reg. 37
Whipps Cross, E.11. H.O. 37
Whittington, N.19. H.O. 37
Birmingham. Moseley Hall Hosp. for Child. Sr. H.O. 38
Carshalton. St. Heller. H.O. .. 38
Manchester. Duchess of York Hosp. for Babies & Wythenshawe. Sr. H.O. 41
Manchester. West Manchester H.M.C. H.O. 41
Stoke-on-Trent. City Gen. Pre-reg. H.O. 44
Warrington Gen. Sr. H.O. 45
Watford. Shrodells. Sr. H.O. .. 44

PATHOLOGY
North East Met. R.H.B. Regs. .. 36
Newcastle R.H.B. Sr. Reg... .. 41
Oxford United Hosps. Sr. H.O. .. 42
Redhill County Hosp. Reg. 42
Winchester Group H.M.C. Reg. .. 44
Worthing Group H.M.C. Reg. .. 44

PSYCHIATRY
North East Met. R.H.B. P.-t. Sr. H.M.O. 34
South East Met. R.H.B. P.-t. Cons... 34
Aberdeen Gen. Hosps. B.O.M. Reg. 37
Bexley, Kent. Sr. H.O. 37
Birmingham R.H.B. Cons. & Sr. H.M.O. 34
Crowthorne, Berks. Broadmoor Institution. Cons. 34
Glasgow. Hawkhead (Mental). Sr. H.O. 39
Isle of Man. Ballamona. Sr. H.O. .. 40
Ivybridge. Moorhaven. Jr. H.M.O. 40
Leeds R.H.B. Cons. 35
Leicester. Towers Mental. Jr. H.M.O. 41
Manchester. Prestwich. Reg. .. 41
Manchester R.H.B. Sr. H.M.O. .. 34
Montrose. Royal Mental. Jr. H.M.O. 41
Newcastle R.H.B. Regs. & Locum Regs. 41
North East Met. R.H.B. Regs. .. 36
Oxford R.H.B. Cons... 35
Retford, Notts. Rampton. Deputy Med. Supt. (Cons.) 35
St. Albans. Harperbury. Reg. .. 44
St. Albans. Napsbury Mental. Sr. H.O. 44
St. Albans. Shenley. Jr. H.M.O. .. 44
West Malling. Leybourne Grange Colony. Locum Jr. H.M.O. .. 44
U.S.A. Virginia. Physicians .. 35

RADIOLOGY
St. Thomas's, S.E.1. Sr. Reg. .. 36
Birmingham R.H.B. Cons. & Sr. H.M.O. 34
East Anglian R.H.B. Reg. 39
Scotland. Western R.H.B. Reg. .. 43

RADIOTHERAPY
Marie Curie, N.W.3. H.O. 36
Royal Marsden, S.W.3. Sr. H.M.O. .. 34
Royal Marsden, S.W.3. Regs. .. 36
Cambridge. Addenbrooke's. Reg. .. 38
Scotland. Western R.H.B. Sr. Reg. 43
Melbourne. Aust. Cancer Institute Board. Cons. 35

RHEUMATOLOGY
Leeds R.H.B. & Univ. of Leeds. Research Reg. 40

SURGERY
Bolingbroke, S.W.11. H.O. 35
Charing Cross Hosp. Group. Reg .. 35
Hosp. for Sick Child., W.C.1. Sr. H.O. 37
Hosp. of St. John & St. Elizabeth, N.W.8. Locum Reg. 36
Royal Marsden, S.W.3. H.O... .. 36
Royal Masonic, W.6. Reg. 36
South East Met. R.H.B. R.S.O. .. 37
St. Ann's Gen., N.15. H.O. 37
St. Charles', W.10. Regs. 37
Whittington, N.19. H.O.'s.. 37
Aberystwyth. Sr. H.O. 37
Accrington. Victoria. H.O. 37
Barnstaple. North Devon Infy. Pre-reg. H.O. 37
Beverley, Westwood. H.O. 37
Birmingham United Hosps. Reg. .. 38
Bishop's Stortford. Herts & Essex Gen. Pre-reg. H.O. 37
Blackpool. Victoria. Pre-reg. H.O. .. 38
Bournemouth. Royal Victoria. H.O. 38
Brighton. Royal Sussex County. Pre-reg. H.O.'s 38
Burton-on-Trent. Gen. Pre-reg. H.O. 38
Carluke, Lanarkshire. Law. H.O. .. 38
Carmarthen. West Wales Gen. Sr. H.O. 39
Carshalton. Queen Mary's Hosp. for Child. H.O... 38
Colchester Group H.M.C. H.O. .. 39
Edgware Gen. H.O. 39
Glasgow. Southern Gen. Sr. H.O... 39
Halifax Gen. Sr. H.O... 40
Hastings. Royal East Sussex. Pre-reg. H.O.'s 39
Herefordshire Group. Reg... .. 39
Huddersfield Royal Infy. H.O. .. 40
Hull. Kingston Gen. Pre-reg. H.O. .. 40
Hull. Kingston Gen. Sr. H.O. 40
Hull. Victoria Hosp. for Sick Child. Locum H.O... 40
King's Lynn. West Norfolk & King's Lynn Gen. H.O. 40
Lincoln County. Pre-reg. H.O.'s .. 41
Liverpool United Hosps. H.O. .. 41
Macclesfield & Dist. H.M.C. Pre-reg. H.O. 41
Manchester. Booth Hall Child's. Sr. H.O. & H.O. 41
Newton Abbot, Devon. Sr. H.O... 41
Northampton Gen. H.O. & Sr. H.O. 42
Nottingham Child's. Sr. H.O. .. 42
Peterborough. Mem. H.O. 42
Romford. Victoria. H.O. 42
Salisbury Gen. Sr. H.O. or H.O. .. 42
Scotland. Eastern R.H.B. Reg. .. 43
Scotland. Western R.H.B. Regs... 43
Shrewsbury. Royal Salop Infy. & Copthorne. H.O. 42
Slough. Upton. Locum Sr. Reg. .. 44
Southampton. Royal South Hants. H.O. 43
Southend Gen. H.O. 43
St. Helens & District H.M.C. H.O. 44
Stoke-on-Trent. City Gen. Pre-reg. H.O. 44
Torquay. Torbay. Sr. H.O. 44
Welsh R.H.B. Regs... 44
Whitehaven, Cumberland. Pre-reg. H.O. or Sr. H.O. 44
Whitehaven, Cumberland. Sr. H.O. or H.O. 44
Wigan & Leigh H.M.C. Pre-reg. H.O.'s 44
Wolverhampton. New Cross. Pre-reg. H.O. 44
B.W.I. University College Hosp. of the West Indies. Reg. 44

THORACIC SURGERY
London Chest, E.2. Sr. H.O. .. 36
London Chest, E.2. Sr. H.O. or Reg. 36
South East Met. R.H.B. Reg. .. 37
Birmingham R.H.B. Reg. 38
Bristol. Cossham & Frenchay H.M.C. Sr. H.O. 38
Southampton Chest Hosp. Sr. Reg. 43

TROPICAL MEDICINE
Queen Mary's, S.W.15. Jr. H.M.O. 36

PUBLIC APPOINTMENTS 45

GENERAL PRACTICE 46

MISCELLANEOUS 46

The Terms and Conditions of Service of Hospital Medical and Dental Staff apply to all N.H.S. hospital posts we advertise, unless otherwise stated. Canvassing disqualifies, but candidates may normally visit the hospital by appointment.

Academic and Educational

THE ROYAL INSTITUTE OF PUBLIC HEALTH AND HYGIENE

THE DIPLOMA IN PUBLIC HEALTH
THE DIPLOMA IN INDUSTRIAL HEALTH

The next COURSES OF INSTRUCTION for the above Diplomas will commence on 20TH SEPTEMBER, 1957. Tuition may be taken whole-time or part-time.

Prospectuses, enrolment forms, and full details may be obtained from the Acting Secretary, 28, Portland-place, London, W.1 (Telephone : LANgham 2731/2).

KING'S COLLEGE HOSPITAL MEDICAL SCHOOL
(UNIVERSITY OF LONDON)
DEPARTMENT OF CHEMICAL PATHOLOGY

MILES AMES FELLOWSHIP IN ENDOCRINOLOGY

Applications are invited for the Miles Ames Fellowship in Endocrinology. Candidates should hold a Ph.D. degree or its equivalent in chemistry, biochemistry or an allied subject. The successful candidate will be required to carry out original work on steroid hormones or on any other aspect of endocrinology in which he or she is particularly competent. Salary not less than £750 p.a., with superannuation.

Applications, with the names and addresses of 3 referees, should be submitted before 14th September, 1957, to the Secretary, King's College Hospital Medical School, Denmark-hill, London, S.E.5, from whom further particulars may be obtained.

SOCIETY OF APOTHECARIES OF LONDON

DIPLOMA IN INDUSTRIAL HEALTH

The next Examination will begin on MONDAY, 9TH DECEMBER, 1957. The following Examination will be held in July, 1958.

For Regulations apply Registrar, Apothecaries' Hall, Black Friars-lane, London, E.C.4.

ALFRED HOSPITAL, Melbourne, S.1, Victoria, Australia

MEDICAL RESEARCH AND TRAVELLING SCHOLARSHIPS

Applications are invited from University graduates for scholarships for 1958.

Successful applicants for research scholarships will normally be required to carry out their work, either part or full time, within the Hospital. Grants may be made to graduates as trainee research workers.

The facilities available for research include general medical and surgical wards, pediatric ward, professorial medical and surgical units, Baker Medical Research Institute (including Clinical Research Unit), Diabetic and Metabolic Unit and routine investigational departments.

The value of the Scholarships awarded will be determined by the standing of the applicant and the time to be devoted to the study. Usually the Scholarships will range from £250 to £2000 p.a., but 1 Scholarship of value £2000–£2500 p.a. for 3 years may be awarded should there be a suitable applicant. Holders of these Scholarships are eligible for further awards in subsequent years.

Applications on the prescribed form, must be lodged by 31st October with the undersigned from whom further information and application forms for either Research or Travelling Scholarships may be obtained on request. Only in exceptional circumstances will applications be considered if received later than the specified date.

The Edward Wilson Memorial Fellowship may be awarded annually to an overseas graduate to enable him to work for a year in Alfred Hospital. Applications should be lodged with the undersigned by 30th June. An overseas graduate appointed to this Fellowship is normally expected to commence duties at some time between 1st January and 31st March of the following year. Although not eligible to hold this Fellowship for a second year the holder may apply for any of the other scholarships mentioned herein should he wish to extend his work beyond a year.

Income for the award of scholarships is derived from the following funds : The Victor Y. and Margaret Kimpton Research Scholarship Fund, the Sol Green Research Scholarship Fund, the J. F. Mackeddie Research Scholarship Fund, the Ringland Anderson Research Scholarship Fund, A. A. Swallow Research Scholarship Fund, E. H. Flack Medical Research Fund, R. B. McComas Memorial Research Fund, the Edward Wilson Memorial Research Fund, George Merriman Fund, Frederick and Esther Michaelis Trust, Neurological Trust Fund, Sydney William Jones Medical Research Foundation, the Marian and E. H. Flack Travelling Scholarship, J. H. Patterson Travelling Scholarship Trust Fund, Alfred Hospital Medical Research Fund, and Alfred Hospital Clinical Research Fund.

C. G. RANKIN, Manager.

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. RESEARCH ASSISTANT required (full-time) to work on pathological and clinical aspects of the study of breast cancer. Appointment for 1 year in the first instance, with a grant according to qualifications and capabilities.

Applications to be sent to the House Governor.

UNIVERSITY OF OXFORD, RADCLIFFE INFIRMARY, DEPARTMENT OF PATHOLOGY. Applications are invited for the post of GRADUATE ASSISTANT in the Department. The successful applicant will take part in the teaching and diagnostic work of the Department ; there will be opportunities for original work. The commencing salary will be within a range from £700 to £1400 (the salary will be increased when the supplementation of academic salaries takes place shortly) according to qualifications and experience, with family allowance and F.S.S.U. Duties to commence in October, 1957.

Applications, together with names of 3 referees, should be sent not later than 2nd September, 1957, to Dr. A. H. T. ROBB-SMITH, Radcliffe Infirmary, from whom further particulars may be obtained.

Hospital Services : Senior Appointments

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

Part-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer grade), to West Essex Child Guidance Clinic, 263, High-street, Walthamstow, E.17, for 5 sessions a week.

Applications (6 copies), and names of 3 referees, should reach the Secretary, 11A, Portland-place, London, W.1, by Saturday, 21st September, 1957.

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. Applications are invited for the full-time appointment of ASSISTANT RADIOTHERAPIST (Senior Hospital Medical Officer grade). Salary £1653 15s. at age 32. Candidates must hold a Diploma in Medical Radiology.

Applications (12 copies), quoting age, education, qualifications and experience and giving the names of 3 referees, should be sent to the House Governor by 30th August, 1957.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Part-time CONSULTANT PSYCHIATRIST to undertake 4 notional half-days a week for child guidance work at the Peckham Child Guidance Unit which is being established at the Queen's-road Centre, St. Mary's-road, S.E.15, under the administration of the London County Council. Candidates must have had previous extensive experience of child guidance. Possession of a D.P.M. is essential and preferably a higher qualification.

Apply, stating nationality, age, sex, qualifications and experience, including details of present appointment and of war service, together with the names and addresses of 3 referees, to the Secretary, Advisory Appointments Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, by 7th September, 1957.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Part-time CONSULTANT PHYSICIAN (8 half-days per week) for the Lambeth Group of hospitals, for duties mainly at Lambeth Hospital, S.E.11.

Applications by letter (5 copies), giving date of birth, qualifications, experience, names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 21st September, 1957. Applicants may visit Hospital by local arrangement.

SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD requires Whole-time PHYSICIAN-SUPERINTENDENT AND CONSULTANT GERIATRICIAN at St. John's Hospital, Battersea, S.W.11. Residence desirable but not essential.

Applications by letter (5 copies), giving date of birth, qualifications, experience, names of 3 referees, to Secretary (S.1), South West Metropolitan Regional Hospital Board, 11A, Portland-place, W.1, by 21st September, 1957. Applicants may visit Hospital by local arrangement.

THE HOSPITAL FOR SICK CHILDREN. Great Ormond-street, London, W.C.1. There will be a vacancy in October, 1957, for a Part-time MEDICAL OFFICER to the Cardio-thoracic Unit (4 sessions per week).

Further particulars and form of application, which must be returned not later than 9th September, 1957, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

Whole-time CONSULTANT RADIOLOGIST. Duties mainly at Dudley Road Hospital (780 Beds) and other group hospitals. Wide experience specialty/higher qualification required.

Whole-time ASSISTANT RADIOLOGIST (£1653 15s.–£2126 5s. p.a.). Duties at Dudley Road Hospital (780 Beds). Diploma Diagnostic Radiology/wide experience specialty essential.

Whole-time CONSULTANT and Whole-time SENIOR HOSPITAL MEDICAL OFFICER in Psychiatry. Duties mainly at St. Edward's Hospital, Cheddleton (1413 Beds). Wide experience specialty required with possession of D.P.M. for Consultant appointment.

Applications (15 copies), stating name, age, nationality, present and previous appointments and details of 3 referees, to Secretary, Regional Hospital Board, 10, Augustus-road, Birmingham, 15, by 23rd September, 1957.

CARDIFF. THE UNITED CARDIFF HOSPITALS. Applications are invited for the appointment of SENIOR CASUALTY OFFICER at the Cardiff Royal Infirmary. Non-resident appointment, to commence as soon as possible, for a period of up to 4 years. Preference given to candidates possessing F.R.C.S. Salary on scale applicable to Senior Hospital Medical Officers.

Application forms are available from the Secretary to the Board, at the Cardiff Royal Infirmary, Newport-road, Cardiff, and should be returned within 14 days of the appearance of this advertisement.

CROWTHORNE, BERKSHIRE. BROADMOOR INSTITUTION. (920 Beds for persons of unsound mind of criminal tendencies.) Whole-time CONSULTANT. Wide experience in psychiatry, and the D.P.M. necessary. Duties may involve attendance at outpatient clinics. House available.

Applications, naming 3 referees, to Medical Superintendent by 7th September, 1957. Candidates may visit Institution by appointment.

MANCHESTER REGIONAL HOSPITAL BOARD. Whole-time ASSISTANT PSYCHIATRIST (Senior Hospital Medical Officer), Prestwich (Mental) Hospital, Manchester (about 3000 Beds). Single person can be accommodated in Hospital, otherwise post non-resident. All modern forms of treatment are undertaken. Candidates should have had wide experience in psychiatry ; D.P.M. desirable.

Application forms from the Senior Administrative Medical Officer to the Board, Cheetwood-road, Manchester, 8, to be returned by 9th September, 1957.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston UPON THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of Locum ASSISTANT ORTHOPÆDIC SURGEON (Senior Hospital Medical Officer grade) for the period 9th–21st September, 1957.

Applications, stating age, qualifications and experience, with 2 recent testimonials, should reach the Physician-Superintendent as soon as possible.

LEEDS REGIONAL HOSPITAL BOARD.

CONSULTANTS in Anæsthetics (maximum part-time sessions):

(i) Hospitals in the East Riding of Yorkshire—mainly at Westwood Hospital, Beverley. 1 session at Hull Royal Infirmary. Person appointed to reside in Beverley.

(ii) Hospitals in the Leeds A and B Groups (mainly at St. James's Hospital). Person appointed to reside in Leeds.

Whole-time CONSULTANT in Psychiatry for duties at Storthes Hall Hospital, Kirkburton, near Huddersfield (2680 Beds). 4-bedroomed detached house available.

CONSULTANT(S) in Child Psychiatry for the York, Scarborough and Harrogate areas—applications are invited from practitioners wishing either to undertake whole-time or maximum part-time service, or a limited number of sessions at any of the 3 undermentioned centres. Applicants for sessional employment should indicate the number of sessions and the area preferred.

The duties to be covered are associated with the York (6 sessions), North Riding (3 sessions) and West Riding (2 sessions) Education Committees, with additional duties in connection with the York Corporation Mental Health Service.

Applications (12 copies), stating age, qualifications and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, by 14th September, 1957.

LEEDS REGIONAL HOSPITAL BOARD. Locum Tenens CONSULTANT or SENIOR HOSPITAL MEDICAL OFFICER in Ophthalmology (8 notional half-days per week), Scarborough and Bridlington. Vacant now—month to month basis.

Applications, stating age, qualifications and details of appointments held showing dates, together with the names and addresses of 3 referees, to the Secretary, Park-parade, Harrogate, as soon as possible.

OXFORD REGIONAL HOSPITAL BOARD. Warneford AND PARK HOSPITALS, OXFORD. Applications are invited for the whole-time or maximum part-time post of CONSULTANT in Child Psychiatry on the establishment of the above hospitals within the Oxford Area Department of Psychiatry. The principal duties are in the field of child psychiatry, and include duties at child guidance clinics and outpatient clinics, and charge of beds for children at the Park Hospital. There will also be some work with adults. Applicants should hold the D.P.M. and a higher qualification in general medicine or pædiatrics is desirable.

Full particulars of the post may be obtained from the Physician-Superintendent, Warneford Hospital, Oxford, and prospective candidates may visit the hospitals and Child Guidance Clinic by arrangement. Applications (12 copies), giving full details and the names of 3 referees, should reach the Secretary, 43, Banbury-road, Oxford, by 30th September, 1957.

RETFORD, NOTTINGHAMSHIRE. RAMPTON HOSPITAL. (1143 Beds for mental defectives of both sexes exhibiting conduct disorders.) Whole-time DEPUTY MEDICAL SUPERINTENDENT (Consultant). Excellent opportunities for study, treatment, and training of behaviour disorders of all kinds and degrees. Wide experience in psychiatry, and the D.P.M., necessary. Post is clinical but experience in hospital administration an advantage. Duties may involve attendance at outpatient clinics. House available. Candidates may visit Hospital by appointment.

Applications, naming 3 referees, to Medical Superintendent by 7th September, 1957.

SHEFFIELD REGIONAL HOSPITAL BOARD. Part-time ASSISTANT ANÆSTHETIST for 3 notional half-days per week required. Grimsby General Hospital. Salary within Senior Hospital Medical Officer scale.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield. Forms to be returned by **21st** September, 1957.

SHEFFIELD REGIONAL HOSPITAL BOARD. Con-SULTANT ORTHOPÆDIC SURGEON (maximum part-time) required. Duties, mainly at Nottingham General Hospital, include responsibility for the conduct of the Casualty Department.

Application forms and further details from Senior Administrative Medical Officer, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, 10. Forms to be returned by 14th September, 1957.

NORTHERN IRELAND HOSPITALS AUTHORITY. Applications are invited for appointment of CONSULTANT OBSTETRICIAN AND GYNÆCOLOGIST at hospitals managed by the Downpatrick, North Down and Downshire Hospital Management Committees. The appointment will be on a part-time basis of 7 half-days of duty weekly and the terms and conditions will be in accordance with the Authority's application of the Spens report to Northern Ireland.

Applications to be made on a form obtainable (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44–46, Queen-street, Belfast, and to be returned not later than 18th September, 1957.

U.S.A. VIRGINIA. Progressive State mental hospital in Virginia. 4600 Beds, expanding staff, invites applications for PHYSICIANS at all levels, psychiatric experience desirable but not necessary. Salary from $8040 (approximately £2750). All modern methods of treatments. Opportunities for research. Good retirement plan.

Apply to JUUL C. NIELSEN, M.D., Superintendent, sending full résumé in first letter to Box 271, Petersburg, Virginia, U.S.A.

MELBOURNE, VICTORIA, AUSTRALIA. CANCER INSTITUTE BOARD. Applications are invited from suitably qualified medical practitioners for the position of CONSULTANT RADIOTHERAPIST. In addition to clinical duties at Melbourne, the appointee will be required to conduct consultative peripheral clinics within the State of Victoria. The Institute has modern equipment for radiotherapy, including a 4 M.E.V. Linear Accelerator, and other well-appointed services for treatment of inpatients and outpatients (18,500 attendances annually). There are facilities for research in the clinical sphere, medical physics and pathology. The full-time salary at commencement will be at the rate of £A3306 6s. 8d. p.a. Other terms of the appointment include: (*a*) Rights to limited private practice under certain conditions; (*b*) Superannuation; (*c*) Long-service leave, recreational and sick leave entitlements. The position is non-resident. An appointee from overseas will be granted first-class fares for himself and family also an allowance of £200 sterling for the transport of furniture and personal effects.

Further information is available from the undersigned with whom applications close on 31st October, 1957.

A. F. CAMERON, Manager and Secretary.

TASMANIA. LAUNCESTON GENERAL HOSPITAL. Applications, in duplicate, addressed to the Agent-General for Tasmania, 457, Strand, London, W.C.2, and closing on 7th September, 1957, are invited from medical practitioners registrable in Tasmania for appointment to the position of DEPUTY SUPERINTENDENT. The position is a full-time appointment to the Launceston General Hospital.

Salary range: £A2000 p.a., rising by annual increments of £A50 p.a. to £A2250 p.a. Preference will be given to applicants with higher qualifications in medicine and in this case the undermentioned salary range will apply. £A2250 p.a. rising by annual increments of £A50 p.a. to £A2500 p.a.

Duties:

(*a*) Administration and general supervision of the Outpatient Department, which includes the responsibility for conducting a daily clinic and advising on the disposal of all patients attending that department.

(*b*) Consultant to the resident medical officers of the Outpatient Department.

(*c*) To attend to matters delegated by the General Superintendent.

(*d*) To have full power of acting as General Superintendent in his absence.

Annual recreation leave—28 days. Superannuation benefits available. A single applicant will be provided with accommodation. In the case of a married applicant, a house could be made available on a rental basis. An assisted passage can be arranged through the Immigration Department or, alternatively, forward fares only will be refunded up to an amount of £500 at the rate of £100 p.a. at the end of each completed year of service.

Further particulars may be obtained from the Agent-General for Tasmania or the General Superintendent, Launceston General Hospital.

Hospital Services : Junior Appointments

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. Locum HOUSE PHYSICIAN, required from **21st** September to 4th October, 1957, inclusive.

Apply Hospital Secretary, enclosing copies of 3 recent testimonials.

BOLINGBROKE HOSPITAL, Wandsworth Common, S.W.11. HOUSE SURGEON (resident), vacant 21st September, 1957. Open to registered practitioners and pre-registration candidates.

Apply to Hospital Secretary, enclosing copies of 3 recent testimonials, by 28th August, 1957.

BROMPTON HOSPITAL, S.W.3. Applications invited for the post of RESIDENT HOUSE PHYSICIAN (3 vacancies). 2 vacancies for 6 months from 1st November, 1957. Duties include work in Outpatient Department and wards. 1 vacancy for 9 months from 1st November, 1957. The first 3 months at Brompton Hospital Sanatorium, Frimley, and the following 6 months at the Hospital in London covering work in Outpatient Department and wards. Salary at the rate of £577 10s. p.a.

Applications, stating age, qualifications with dates, nationality and appointments held, together with copies of testimonials, by 7th September, 1957, to—

KENNETH A. F. MILES, House Governor.

CHARING CROSS HOSPITAL GROUP. Wembley HOSPITAL. (134 Beds.) SURGICAL REGISTRAR (resident). Tenable for 1 year in the first instance from 1st October, 1957. Candidates should hold the Diploma of F.R.C.S.

Applications, with copies of testimonials and names of 2 referees, to reach the undersigned by 7th September, 1957.

FRANK HART, Secretary to the Board.

Charing Cross Hospital, Strand, W.C.2.

CONNAUGHT HOSPITAL, Walthamstow, E.17. (123 Beds.) Applications are invited for the post of SECOND CASUALTY OFFICER with duties in the Department of Orthopædic and Traumatic Surgery (Senior House Officer grade). Recognised for F.R.C.S. Salary £819 10s. p.a., less £150 p.a. for board, lodging, &c.

Applications, with full details and copies of 2 recent testimonials, to be sent immediately to Secretary, Forest Group Hospital Management Committee, Langthorne-road, E.11.

EASTERN HOSPITAL, London, E.9. (Fevers.) Applica-tions are invited for appointment as registered RESIDENT HOUSE PHYSICIAN. Duties may include some work in Chest Unit. Facilities for postgraduate study for higher qualifications.

Apply Group Secretary, Hackney Hospital, London, E.9, by 6th September, quoting EH/HO.

HAMMERSMITH HOSPITAL AND POSTGRADUATE MEDICAL SCHOOL, Ducane-road, London, W.12. SENIOR REGISTRAR (anæsthetics) required.

Applications, stating age, qualifications, experience, names of 2 referees, to Secretary, Board of Governors, by 7th September.

GUY'S HOSPITAL, S.E.1. Applications are invited for the post of Part-time REGISTRAR (mid-grade) to the Endocrine and B.M.R. Department, with duties on 7 sessions per week, commencing 1st October, 1957.

Forms of application are obtainable from, and should be lodged with, the Superintendent, Guy's Hospital, London Bridge, S.E.1, not later than 5th September, 1957.

HAMPSTEAD GENERAL HOSPITAL, Haverstock Hill, N.W.3. (ROYAL FREE HOSPITAL GROUP.) Applications are invited from registered medical practitioners for the post of RESIDENT CASUALTY OFFICER (graded as Senior House Officer). Salary £819 10s. p.a. Vacant 1st September, 1957, tenable for a period of 6 months at the Main Outpatients Department, Bayham-street, N.W.1.

Application forms may be obtained from the Secretary, to whom they should be returned, together with copies of 3 recent testimonials, immediately.

HENDON ISOLATION HOSPITAL, Goldsmith-avenue, London, N.W.9. (92 infectious diseases beds and 20 gynæcological beds.) Locum JUNIOR HOSPITAL MEDICAL OFFICER required from 1st September, 1957, for an indefinite period at above Hospital.

Apply immediately to Physician-in-charge (telephone : COLindale 8182).

HENDON ISOLATION HOSPITAL, Goldsmith-avenue, London, N.W.9. (92 infectious diseases beds and 20 gynæcological beds.) JUNIOR HOSPITAL MEDICAL OFFICER (resident) required at above Hospital. Previous similar experience essential.

Apply, stating age, nationality, qualifications and details of experience, together with the names and addresses of 2 referees, to Group Secretary, Edgware General Hospital, Edgware, Middlesex, by 7th September, 1957.

HOSPITAL OF ST. JOHN AND ST. ELIZABETH, 60, Grove End-road, London, N.W.8. Locum Tenens Full-time SURGICAL REGISTRAR (Male) required immediately. The possession of the Diploma of Fellow of 1 of the Royal Colleges is essential.

Further particulars may be obtained from the Secretary to whom applications, with names of 3 referees, should be sent.

LAMBETH HOSPITAL, Brook-drive, S.E.11. Applications are invited from pre-registration and registered medical practitioners for the post of RESIDENT HOUSE PHYSICIAN, vacant 1st October, 1957. The successful candidate will be expected to carry out a fortnight's Locum duty from 17th September, 1957.

Application forms from the Acting Physician-Superintendent. A self addressed envelope should be enclosed.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. A vacancy occurs 1st November, 1957, for RESIDENT HOUSE SURGEON at the Hospital's Country Branch, near Hitchin and Letchworth, Herts. The post is graded as Senior House Officer and the appointment, which provides excellent opportunities for experience in thoracic surgery, is for 6 months.

Applications from registered medical practitioners, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 20th September.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases of THE CHEST. A vacancy occurs 1st November for RESIDENT SURGICAL OFFICER. Appointment for 6 months, with prospect of renewal. Post graded as Senior House Officer or Registrar, according to qualifications and previous surgical experience.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 20th September.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON CHEST HOSPITAL. Hospitals for Diseases OF THE CHEST. Applications are invited for the post of MEDICAL REGISTRAR. The appointment is for 1 year in the first instance and is non-resident. Duties include ward rounds, outpatient clinics and attendance at the Country Branch, near Letchworth.

Applications, stating date of birth, qualifications with dates, and previous appointments held, with copies of 3 testimonials, should reach the undersigned not later than 14th September.

THOMAS BROWN, House Governor.

London Chest Hospital, E.2.

LONDON HOSPITAL, Whitechapel, E.1. Applications are invited for the post of REGISTRAR to the Department of Anæsthetics. D.A. or D.A. standard an advantage.

Applications (12 copies), giving the names and addresses of 3 referees, should be received by the undersigned by 6th September, 1957. H. BRIERLEY, House Governor.

MARIE CURIE HOSPITAL, 66, Fitzjohn's-avenue, Hampstead, N.W.3. GYNÆCOLOGICAL HOUSE SURGEON (radiotherapy), resident, required immediately.

Applications, with copies of testimonials, to the Administrative Officer.

NATIONAL HEART HOSPITAL, Maida Moreton, Buckingham. (Country Branch of the National Heart Hospital.) Applications are invited for the post of RESIDENT MEDICAL OFFICER at the Hospital's Country Branch. The appointment is for a period of 6 months from 1st October, 1957, but may be renewed for a further period not exceeding 6 months. The status of the post is that of a Senior House Officer and the salary is in accordance with the terms and conditions of service. The holder will be expected to attend on 1 day weekly at the Hospital in Westmoreland-street.

Applications, with copies of 3 recent testimonials, should be sent to me at Westmoreland-street, London, W.1, not later than 31st August, 1957.

ROBERT G. E. WHITNEY, Secretary to the Board.

NATIONAL HEART HOSPITAL, Westmoreland-street, London, W.1 (with which is associated the Institute of Cardiology). Applications are invited for the post of RESIDENT MEDICAL OFFICER (Male). The appointment is for a period of 6 months from 1st October, 1957, but may be renewed for a further period of 6 months. The status and salary are either that of a Senior House Officer or Registrar and are in accordance with the national terms and conditions of service.

Applications, with copies of 3 recent testimonials, should be sent to me not later than Saturday, 31st August, 1957.

ROBERT G. E. WHITNEY, Secretary to the Board.

NATIONAL TEMPERANCE HOSPITAL, Hampstead-road, N.W.1. (General Hospital—158 Beds.) Applications are invited for the post of Whole-time ANÆSTHETIC REGISTRAR (resident, or non-resident if residing close to Hospital). Hospital may be visited by direct appointment. The post is recognised for the F.F.A.R.C.S. and the successful candidate will have access to a Maternity Unit and a Chest Unit in other General Hospitals in the Group.

Application forms obtainable from, and returnable to, the Secretary to Committee, Paddington Group Hospital Management Committee, 285, Harrow-road, W.9, by 10th September.

NEASDEN HOSPITAL, Brentfield-road, Neasden, N.W.10. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Whole-time Locum Tenens MEDICAL REGISTRAR (resident) required from 23rd September, 1957, to 6th October, 1957, inclusive. Experience in infectious diseases and children's diseases an advantage. The Hospital is a Regional Centre for poliomyelitis.

Applications to Physician-Superintendent.

NORTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD.

PSYCHIATRIC REGISTRAR (resident or non-resident), Goodmayes Hospital, Ilford, Essex. Recognised for D.P.M.

REGISTRAR in Mental Deficiency (non-resident. Unfurnished house available in Colchester), Royal Eastern Counties Hospital, Colchester, Essex. Recognised for 1 year for D.P.M.

MEDICAL REGISTRAR (resident, or non-resident sleeping in on duty nights), St. Andrew's Hospital, Bow, E.3. Experience in pædiatrics an advantage.

E.N.T. SURGICAL REGISTRAR (non-resident), Whipps Cross Hospital, Leytonstone, E.11. Some duties at Park House Health Centre E.N.T. Clinic, E.10.

REGISTRAR in Pathology (non-resident), Group Laboratory, Southend-on-Sea Group of hospitals, Essex. Post offers excellent facilities for training in all branches of pathology and is recognised for Diploma in Pathology. Vacant 12th October.

REGISTRAR in Pathology (resident, or non-resident near Hospital), Whipps Cross Hospital, Leytonstone, E.11. Recognised for Diploma in Pathology.

Appointments subject to review after 1 year.

Application forms from Secretary, 11A, Portland-place, W.1, to be returned by 7th September, 1957.

POSTGRADUATE MEDICAL SCHOOL AND HAMMERSMITH HOSPITAL. Required, REGISTRAR (hæmatology), 1st October, for routine work, including transfusion and teaching in D.C.P. course. Opportunities for research. Terms of appointment similar to National Health Service.

Apply, with names of 2 referees, to the Dean, Postgraduate Medical School, Ducane-road, W.12, by 9th September, 1957.

QUEEN MARY'S HOSPITAL, Roehampton, London, S.W.15. (376 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (Tropical Unit) required immediately. National Health Service terms and conditions.

Apply Medical Superintendent.

ROYAL FREE HOSPITAL, Gray's Inn-road, London, W.C.1. Applications are invited for the post of SENIOR E.N.T. REGISTRAR. The appointment will be for 1 year in the first instance and subject to annual review. Duties to commence as soon as possible.

Applications with names of 3 referees, to be forwarded to the Administrator within 14 days.

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. Applications are invited for 2 full-time posts of REGISTRAR in the Radiotherapy Department. Salary £935 a year. Candidates not holding a Diploma in Medical Radiology will be considered, especially if they have a higher qualification in medicine or surgery.

Forms of application are obtainable from the House Governor, to whom applications, together with the names of 3 referees, should be sent by 30th August, 1957.

ROYAL MARSDEN HOSPITAL, Fulham-road, S.W.3. Applications are invited from registered medical practitioners for the post of HOUSE SURGEON (resident). Salary £577 10s. a year. The post is tenable for 6 months from 3rd November, 1957.

Forms of application are obtainable from the House Governor, to whom applications, together with copies of 3 recent testimonials, should be sent, not later than 30th August, 1957.

ROYAL MASONIC HOSPITAL, Ravenscourt Park, London, W.6. Applications are invited for the post of RESIDENT SURGICAL REGISTRAR. Appointment about 1st October, 1957. Gross salary : first year £935 (residential emoluments of £130 deductible) ; second year £1061 10s. (residential emoluments of £145 deductible).

Please state age, qualifications, past and present appointments and include 2 recent testimonials and/or the names of 2 referees. Applications should reach the undersigned (from whom further information may be obtained) as soon as possible, and in any event not later than 14th September, 1957.

R. E. LAWSON, Secretary and House Governor.

ST. THOMAS'S HOSPITAL, London, S.E.1. Senior REGISTRAR to the X-ray Diagnostic Department. Whole-time, for a period of 1 year in the first instance.

Applications, naming 2 referees, to the Clerk of the Governors by 3rd September, 1957.

ST. ANN'S GENERAL HOSPITAL, N.15. Applications are invited for the appointment of RESIDENT HOUSE SURGEON (third post) to above Hospital, for a period of 6 months. Vacant immediately.

Application form from Secretary, Tottenham Group Hospital Management Committee, The Green, N.15.

ST. CHARLES' HOSPITAL, Ladbroke-grove, W.10. (577 Beds.) Applications are invited for the posts of 2 Whole-time SURGICAL REGISTRARS, vacant on 1st October and 7th November respectively. (Resident preferred for post vacant on 1st October.) Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Secretary to Committee, Paddington Group Hospital Management Committee, Harrow-road, W.9, by 10th September.

ST. JAMES' HOSPITAL, Balham, London, S.W.12. WANDSWORTH HOSPITAL GROUP. Applications are invited for the post of HOUSE SURGEON (gynæcological), vacant mid-September.

Applications, stating age, qualifications, experience and the names and addresses of 2 referees, to the Group Secretary at above address by 2nd September, 1957. (0385.)

ST. STEPHEN'S HOSPITAL, Chelsea, S.W.10. House PHYSICIAN. Post-registration. Resident. General medicine and some tuberculosis. Vacancy late September, 1957.

Applications, naming 2 referees, to Medical Superintendent.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for a whole-time appointment as RESIDENT SURGICAL OFFICER to fill a vacancy in the approved establishment at the Woolwich Group of hospitals, available on 1st November, 1957. The successful candidate will be required to reside at St. Nicholas Hospital, Tewson-road, Plumstead, S.E.18. The salary will be £1061 10s. p.a. and the appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance, renewable for a further year.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 7th September, 1957.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Thoracic Surgery for duty at the Regional Thoracic Unit at the Brook General Hospital, Shooters Hill, S.E.18, and also at Grove Park Hospital, Marvels-lane, Lee, S.E.12. The work includes both tubercular and non-tubercular chest surgery. The appointment which will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance, is available on 14th October, 1957.

Applications, giving particulars of age, qualifications, and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 7th September, 1957.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. Applications are invited for the post of Whole-time SENIOR REGISTRAR to the E.N.T. Department, falling vacant on 1st November, 1957.

Further particulars and form of application, which must be returned not later than Monday, 9th September, 1957, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

THE HOSPITAL FOR SICK CHILDREN, Great Ormond-street, London, W.C.1. There will be vacancies for the following Senior House Officers :—

1 HOUSE PHYSICIAN—on 15th November, 1957.
1 HOUSE SURGEON to the Orthopædic and Plastic Departments—on 15th November, 1957.

Further particulars and form of application, which must be returned not later than 9th September, 1957, are obtainable from the undersigned.

H. F. RUTHERFORD, House Governor and Secretary.

WESTMINSTER CHILDREN'S HOSPITAL. WESTMINSTER HOSPITAL TEACHING GROUP. Applications are invited for the post of SENIOR MEDICAL REGISTRAR (non-resident) from 1st November, 1957.

Apply, naming 3 referees, to the Secretary, Westminster Children's Hospital, Vincent-square, S.W.1, by 21st September, 1957.

WHITTINGTON HOSPITAL, London, N.19. Locum Tenens E.N.T. REGISTRAR required from 2nd to 15th September, 1957.

Write or call Medical Superintendent (ARC 3070, Ext. 440).

WHITTINGTON HOSPITAL, London, N.19. Applications are invited for the following appointments :—

*HOUSE PHYSICIAN (general medicine), 5 posts. Recognised for M.D. (Lond.).
* HOUSE PHYSICIAN (pædiatric). Recognised for M.D. (Lond.) and D.C.H.
* HOUSE PHYSICIAN (geriatric).
† HOUSE SURGEON (general surgery), 2 posts. Recognised for F.R.C.S. (Eng.).
* HOUSE SURGEON (obstetric), 2 posts. Recognised for M.R.C.O.G. in obstetrics.

All posts vacant 1st October, 1957.

* Pre-registration candidates who have already held a first appointment may apply.

† Pre-registration candidates may apply.

Application forms obtainable from the Group Secretary, 46, Cholmeley-park, N.6 (ARC 3070, Ext. 527), and returnable to the Medical Superintendent, Whittington Hospital, London, N.19, by 2nd September, 1957.

WHIPPS CROSS HOSPITAL, London, E.11. Leytonstone (NO. 10) HOSPITAL GROUP. Applications are invited for the post of PÆDIATRIC HOUSE PHYSICIAN (post-registration) at above Hospital. The post, which is recognised for D.C.H., becomes vacant on 1st October, 1957.

Application forms from the Hospital Secretary, to be returned by 31st August, 1957.

ABERDEEN GENERAL HOSPITALS BOARD OF MANAGEMENT. Applications are invited for the appointment of REGISTRAR in the Department of Psychological Medicine, at the Aberdeen Royal Infirmary. Conditions of service in accordance with the terms issued by the Department of Health for Scotland.

Applications, with the names of 2 referees, to be lodged with the Group Secretary and Treasurer, Aberdeen General Hospitals, P.O. Box No. 92, 62, Queen's-road, Aberdeen, within 14 days of the appearance of this advertisement.

ABERYSTWYTH, CARDIGANSHIRE. GENERAL HOSPITAL. SENIOR HOUSE OFFICER (surgical) required (resident). Post recognised for F.R.C.S. examination. Vacancy from 1st October, 1957.

Applications, stating age and experience, &c., to the Group Secretary, Mid-Wales Hospital Management Committee, 31, North-parade, Aberystwyth, Cards.

ACCRINGTON. VICTORIA HOSPITAL. (114 Beds.) BLACKBURN AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required for 6th September, 1957. Post recognised for F.R.C.S. and approved for pre-registration purposes.

Applications to Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn.

AYLESBURY, BUCKINGHAMSHIRE. STOKE MANDEVILLE HOSPITAL. (619 Beds.) Applications are invited for the post of RESIDENT HOUSE PHYSICIAN in the Department of Medicine. Pre-registration post but registered practitioners may apply. Duties include responsibility for 20 acute medical beds and 15 tuberculosis beds. Post vacant 18th September, 1957.

Applications, with copies of 2 testimonials, to the Administrative Officer.

AYLESBURY. ROYAL BUCKINGHAMSHIRE HOSPITAL. Locum CASUALTY OFFICER (Senior House Officer) for period 15th–29th September.

Apply, with copies of 2 recent testimonials, to Secretary-Superintendent as soon as possible.

BARNSTAPLE. NORTH DEVON INFIRMARY. (105 Beds.) HOUSE SURGEON (pre-registration) required. Post vacant 4th September, 1957.

Applications to Group Secretary, North Devon Hospital Management Committee, 19, Alexandra-road, Barnstaple.

BENENDEN CHEST HOSPITAL (Civil Service Sana-TORIUM SOCIETY), BENENDEN, near CRANBROOK, KENT. SENIOR HOUSE OFFICER (resident). Vacancy in mid-September, 1957. Applications are invited from registered medical practitioners, Male or Female. Salary £650 p.a. (10% increase not yet added but under review) with free board and lodgings. The Hospital is independent of the National Health Service. Superannuation scheme in operation. This chest hospital of 169 Beds is fully equipped for the treatment, including regular major thoracic surgery, of adult male and female patients with pulmonary disease, tuberculous and non-tuberculous.

Applications, stating age, qualifications, previous experience, with copies of testimonials, should be sent to the Chief Medical Officer as soon as possible.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 acute beds.) HOUSE SURGEON (first, second or third post), vacant soon. General surgical duties, some orthopædics. Offering good opportunities for general experience in busy acute general hospital. Recognised for F.R.C.S. Approved pre-registration post. Married quarters may be available.

Applications to Group Secretary.

BEVERLEY, YORKSHIRE. WESTWOOD HOSPITAL. (229 acute beds.) ORTHOPÆDIC HOUSE SURGEON (first, second or third post), vacant now. Offers good opportunity for general experience in busy acute general hospital. Approved pre-registration post. Fully qualified practitioners may apply. Recognised for F.R.C.S.

Apply Group Secretary.

BEXLEY HOSPITAL, Dartford Heath, Bexley, Kent. BEXLEY HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for appointment of SENIOR HOUSE OFFICER at above Hospital. Salary £819 10s. p.a., with deductions of £150 p.a. for board, lodging, &c., if resident. The Hospital (2300 Beds) deals with all types of psychiatric illness and experience in all modern physical, occupational, and psychotherapeutic procedure is available. Opportunities will be available to assist at outpatients clinics.

Applications, with names and addresses of 3 referees, should be sent to the Physician-Superintendent, Dr. L. C. COOK, M.D., D.P.M., within 14 days of the appearance of this advertisement.

BISHOP'S STORTFORD, HERTFORDSHIRE. HERTS AND ESSEX GENERAL HOSPITAL. (400 Beds.) Applications are invited for the post of HOUSE OFFICER (surgical), pre-registration. Salary £467 10s.–£522 10s. p.a., less £125 in respect of residential emoluments. Appointment to commence immediately.

Applications, stating age, nationality, qualifications, and experience, with copies of 2 recent testimonials or the names of referees, to the Hospital Secretary.

BIRMINGHAM. THE SKIN HOSPITAL, INPATIENTS' DEPARTMENT, George-road, BIRMINGHAM, 15. SENIOR HOUSE OFFICER or HOUSE OFFICER (resident) required. Modern well-equipped Inpatients' Department, providing facilities for study of skin diseases. Required to assist Consultant at outpatients clinics.

Applications, with copies of 2 recent testimonials, to Group Secretary, Dudley Road Hospital, Birmingham, 18.

BIRMINGHAM, 18. DUDLEY ROAD HOSPITAL. (780 Beds.) SENIOR HOUSE OFFICER (anæsthetics), resident. Recognised for D.A. and F.F.A.R.C.S. Extensive experience of anæsthetics not necessary. Duties include list and emergency work in general surgery, gynæcology, obstetrics and E.N.T. at hospitals in the Group.

Detailed applications, with copies of 3 recent testimonials, to the Group Secretary.

BIRMINGHAM. MOSELEY HALL HOSPITAL FOR CHILDREN, Alcester-road, BIRMINGHAM, 13. (65 Beds.) SENIOR HOUSE OFFICER (pædiatric), now vacant. Resident/non-resident. Recognised for D.C.H.

Apply immediately with 3 testimonials to Secretary, Birmingham (Selly Oak) Hospital Management Committee, Oak Tree-lane, Birmingham, 29.

BIRMINGHAM REGIONAL HOSPITAL BOARD.

Birmingham (Sanatoria) Group, Yardley Green Hospital, Birmingham, 9

REGISTRAR (Thoracic Surgical Unit—66 Beds) for Yardley Green Hospital. Resident or non-resident. Tuberculous and non-tuberculous surgery undertaken. Experience in general surgery essential.

Coventry No. 20 Group, Coventry and Warwickshire Hospital, Coventry

REGISTRAR (obstetrics and gynæcology) for Coventry and Warwickshire Hospital (354 Beds). Resident. Experience specialty essential. Higher qualification desirable. Hospital recognised for M.R.C.O.G./D.Obst.R.C.O.G. and by Birmingham University for clinical teaching.

Application forms from Group Secretaries to be returned by 2nd September, 1957.

BIRMINGHAM (SANATORIA) GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER at West Heath Hospital, Rednal-road, Birmingham, 31, vacant 16th September, 1957 (205 Beds for the treatment of tuberculous and non-tuberculous chest cases). The successful applicant will reside at the above Hospital (accommodation for single person only), and will be offered facilities for undertaking duties at the Birmingham Chest Clinic, Great Charles-street, Birmingham, 3.

Applications, stating age, qualifications, training and experience, together with copies of 3 recent testimonials, should be addressed to the Group Secretary, Birmingham (Sanatoria) Group Hospital Management Committee, Yardley Green Hospital, Birmingham, 9.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE CHILDREN'S HOSPITAL, Ladywood-road, BIRMINGHAM, 16. Applications are invited for the post of SURGICAL REGISTRAR (non-resident), vacant 29th September, 1957. Excellent opportunities exist for performance of pædiatric surgery in close association with the Consultant Surgeons of the Teaching Hospital. Preference will be given to candidates holding a higher qualification. Residence in the Hospital will be required when the Resident Surgical Officer is absent.

Forms of application may be obtained from the House Governor and should be returned not later than 7th September, 1957. G. A. PHALP, Secretary to the Board of Governors.

BIRMINGHAM. THE UNITED BIRMINGHAM HOSPITALS. THE BIRMINGHAM MATERNITY HOSPITAL. Applications are invited from registered medical practitioners for the post of RESIDENT OBSTETRIC HOUSE SURGEON, vacant 1st November, 1957. The appointment is recognised for the M.R.C.O.G. and D.Obst.R.C.O.G.

Application forms obtainable from the House Governor, the Birmingham and Midland Hospitals for Women, Showell Green-lane, Sparkhill, Birmingham, 11, to be returned not later than 2nd September, 1957. G. A. PHALP, Secretary.

BRIGHTON. ROYAL SUSSEX COUNTY HOSPITAL. (312 Beds.)

2 HOUSE PHYSICIANS end of September and October. Pre-registration.

2 HOUSE SURGEONS beginning and end of October. Pre-registration and recognised for F.R.C.S.

Applications, stating usual particulars, and naming 2 referees, to the Administrative Officer, Royal Sussex County Hospital, Brighton, 7.

BRISTOL. COSSHAM AND FRENCHAY HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER required for the Department of Thoracic Surgery (120 Beds) at Frenchay Hospital.

Apply to Group Secretary, Frenchay Hospital, Bristol, giving age and experience and quoting 2 referees.

BROXBURN, WEST LOTHIAN. BANGOUR GENERAL HOSPITAL. Applications are invited for the post of RESIDENT CASUALTY OFFICER (Senior House Officer grade). Salary £819 10s. p.a., less £150 p.a. residential emoluments.

Applications, stating age, qualifications and particulars of previous experience, to the Group Secretary and Treasurer, Board of Management, Bangour Hospital, Broxburn, West Lothian.

BROXBURN, WEST LOTHIAN. BANGOUR GENERAL HOSPITAL. Applications are invited for the post of RESIDENT REGISTRAR in Anæsthetics. Post recognised for D.A.

Applications, naming 2 referees, to the Group Secretary and Treasurer, Board of Management, Bangour Hospital, Broxburn, West Lothian, within 10 days.

BURTON-ON-TRENT. THE GENERAL HOSPITAL. HOUSE SURGEON (general and pre-registration) required at the above Hospital as from 1st September, 1957. Post recognised for F.R.C.S.

Applications to Group Secretary as soon as possible.

BURTON-ON-TRENT. GENERAL HOSPITAL. Junior HOSPITAL MEDICAL OFFICER ANÆSTHETIST required at the above Hospital.

Applications to Group Secretary, General Hospital, Burton-on-Trent, as soon as possible.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) SENIOR HOUSE OFFICER (casualty and traumatic surgery), required for 1st October, 1957. Recognised for F.R.C.S. and offering wide variety of experience.

Applications, stating age, qualifications and experience, and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE OFFICER (obstetrics and gynæcology). Resident pre-registration post recognised for Membership and Diploma of the R.C.O.G. available from 12th November, 1957.

Applications, stating age, experience and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE OFFICER (orthopædic and traumatic surgery). Resident pre-registration post recognised for F.R.C.S. available from 1st October, 1957, in the main acute general hospital serving the Blackpool and Fylde area.

Applications, stating age, experience (if any), and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE PHYSICIANS. 2 resident pre-registration posts available on 1st October, 1957, in the Department of Medicine.

Applications, stating age, experience (if any), and giving the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BLACKPOOL. VICTORIA HOSPITAL. (354 Beds.) HOUSE SURGEON. Resident pre-registration post available on 1st October, 1957, in the Department of Surgery at this modern well-equipped Hospital with excellent facilities for gaining experience. Recognised for F.R.C.S.

Applications, stating age, experience, and the names and addresses of 2 referees, should be sent to the Hospital Secretary.

BOLTON. THE ROYAL INFIRMARY. (238 Beds.) BOLTON AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. RESIDENT SENIOR HOUSE OFFICER in Orthopædic Surgery. Tenable for 12 months and recognised for F.R.C.S.

Applications, stating age, nationality, qualifications, experience, and the names of 2 referees, should be sent immediately to Group Secretary, The Royal Infirmary, Bolton.

BOURNEMOUTH. ROYAL VICTORIA HOSPITAL, Shelley-road. BOURNEMOUTH AND EAST DORSET HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the appointment of GENERAL HOUSE SURGEON. The appointment, which becomes vacant on 7th October, 1957, is recognised for the F.R.C.S. examination and for pre registration purposes.

Applications to the Hospital Secretary.

CAERPHILLY HOSPITAL. (226 Beds for acute general medicine and surgery.) Pre-registration HOUSE OFFICER (orthopædics and general surgery) required at above Hospital.

Apply immediately, with names of referees, to the Group Secretary, Rhymney and Sirhowy Valleys Hospital Management Committee, Central Offices, Caerphilly-road, Ystrad Mynach, Glam.

CAMBRIDGE. ADDENBROOKE'S HOSPITAL. REGISTRAR (non-resident) for Radiotherapeutic Centre. Appointment for 1 year in the first instance, renewable for second year.

Apply, with full particulars and names of 3 referees, to Secretary by 7th September.

CAMBRIDGE. ADDENBROOKE'S HOSPITAL. Locum MEDICAL REGISTRAR for 1 month from 1st September.

Apply at once, with full particulars and names of 2 referees, to Secretary.

CARDIFF. ST. DAVID'S HOSPITAL. Senior House OFFICER required for Accident Unit at above Hospital.

Form of application from Group Secretary, Cardiff Hospital Management Committee, 44, Cathedral-road, Cardiff.

CARLUKE, LANARKSHIRE. LAW HOSPITAL. Applications are invited for the following resident posts (pre- or post-registration) for the 6 months commencing immediately.

HOUSE OFFICER (orthopædic).

HOUSE OFFICER (surgical).

Applications, stating age, qualifications and previous experience, together with the names of 2 referees, should be submitted to the Group Medical Superintendent, Law Hospital, Carluke.

CARSHALTON, SURREY. QUEEN MARY'S HOSPITAL FOR CHILDREN. (A general children's hospital of 700 Beds.) HOUSE SURGEON (House Officer), resident, required for 6 months. (3 months general surgery, 3 months E.N.T. and orthopædics.) Applicants must have completed 12 months Pre-registration Service.

Applications, stating age and qualifications, together with 1 recent testimonial and the names of 2 referees, should be submitted to the Group Secretary immediately.

CARSHALTON, SURREY. ST. HELIER HOSPITAL. PÆDIATRIC HOUSE OFFICER (not pre-registration). Duties in sick children's wards and Neo-natal Department. Post recognised for D.C.H. Successful applicant will be required to start on 19th October.

Apply immediately, giving age, qualifications and experience, with copies of recent testimonials and names of 2 referees, to the Secretary.

CREWE AND DISTRICT MEMORIAL HOSPITAL. (108 Beds Acute, and Continuation 32 Beds.) JUNIOR HOSPITAL MEDICAL OFFICER (anæsthetics), temporary or permanent. D.A. preferred. New operating suite. Duties chiefly at general hospital and a Maternity Unit at another hospital. Hospital approved for D.A. Salary and conditions as per regulations.

Applications, giving age, details of experience, and names of 3 referees, to be sent immediately to Group Secretary, South Cheshire Hospital Management Committee, Barony Hospital, Nantwich, Cheshire.

CARMARTHEN. WEST WALES GENERAL HOSPITAL. (188 Beds.) WEST WALES HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (surgical) (recognised by the Royal College of Surgeons) which is now vacant. Salary and conditions of service as laid down by the Ministry of Health.

Applications, stating age, qualifications, experience and nationality, with names and addresses of 3 referees, to the Group Secretary, West Wales Hospital Management Committee, Glangwili, Carmarthen.

CHERTSEY, SURREY. ST. PETER'S HOSPITAL (late Botley's Park War Hospital). (430 Beds.) Locum SENIOR HOUSE OFFICER ANÆSTHETIST required from 31st August, 1957, to 13th September, 1957.

Applications to Physician-Superintendent, St. Peter's Hospital, as soon as possible.

CHESTERFIELD ROYAL HOSPITAL. Casualty Officer (House Officer or Senior House Officer) required 30th September, 1957. Post recognised for the F.R.C.S. and pre-registration purposes.

Apply, with copies of 2 testimonials, to—
M. H. BOONE, Group Secretary.

COLCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for following posts :—

Essex County Hospital, Colchester, Essex (185 Beds) HOUSE OFFICER (surgical). First, second, third or pre-registration post, tenable for 6 months. Recognised for F.R.C.S.

Black Notley Hospital, Braintree, Essex (516 Beds) HOUSE OFFICER (orthopædic surgery). Duties include care of cases from London Hospital Orthopædic Department. First, second, third or pre-registration post, tenable for 6 months. Recognised for F.R.C.S.

Locum ORTHOPÆDIC REGISTRAR with some duties at the London Hospital from 24th August to 6th October.

Applications, with copies of 3 testimonials, to Group Secretary, Colchester Hospital Management Committee, 14, Pope's-lane, Colchester, Essex.

DERBY. CITY HOSPITAL. Derby Area No. 1 Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of HOUSE PHYSICIAN (pre-registration) or SENIOR HOUSE OFFICER (medical). Post vacant 11th September.

Applications, stating full details, together with copies of 2 recent testimonials, should be sent to the Medical Superintendent, City Hospital, Derby, as soon as possible.

DEWSBURY, YORKSHIRE. STAINCLIFFE GENERAL HOSPITAL. (311 Beds.) Applications are invited for the post of RESIDENT MEDICAL OFFICER (Junior Hospital Medical Officer grade) which becomes vacant on 1st October, 1957. The appointment is tenable for 1 year in the first instance. The Hospital has an acute Medical Unit of 70 Beds. There are 2 House Physicians. Temporary accommodation for an officer who is married could be made available if required.

Applications, giving full details and the names of 3 referees, should be made to the Administrative Officer at the Hospital as soon as possible.

DONCASTER ROYAL INFIRMARY. Doncaster Hospital MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER in Ophthalmology. Recognised for D.O. Post vacant on or about 1st October.

Applications to the Group Secretary at Doncaster Royal Infirmary.

EAST ANGLIAN REGIONAL HOSPITAL BOARD. RADIOLOGICAL REGISTRAR, Ipswich and East Suffolk Hospital (Anglesea Road Wing), Ipswich. The Department is the centre for Consultant Radiological Services for the Ipswich Hospital Group. Post recognised for D.M.R.D. Part II examination. Appointment for 1 year, renewable for second year.

Applications, stating age, experience and the names of 3 referees, to the Board's Senior Administrative Medical Officer, 117, Chesterton-road, Cambridge, by 2nd September, 1957. Candidates are invited to visit Hospital by direct arrangement with the Hospital Management Committee Secretary at the Hospital.

EAST FIFE HOSPITALS BOARD OF MANAGEMENT. CRAIGTOUN MATERNITY HOSPITAL, ST. ANDREWS (48 Beds), NETHERLEA MATERNITY HOSPITAL, NEWPORT (17 Beds). OBSTETRICAL AND GYNÆCOLOGICAL REGISTRAR (resident) for the above North Fife Hospitals required on 1st November, 1957. The post is recognised for training for the M.R.C.O.G. An unfurnished house is available to rent in the hospital grounds at Craigtoun if desired.

Apply, in writing, giving the names of 3 referees, to the Medical Superintendent, East Fife Hospitals Board of Management, 243A, High-street, Kirkcaldy.

EXETER. ROYAL DEVON AND EXETER HOSPITAL. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER (Fracture Department), vacant 16th September, 1957.

Apply, with copies of 2 recent testimonials, to the Hospital Secretary by 7th September, 1957.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. RESIDENT HOUSE SURGEON for above Hospital. Post vacant 6th October. 1957. 6 months appointment. Recognised for F.R.C.S. and pre-registration purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials, to Medical Director of Hospital by 31st August, 1957.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. (702 Beds.) NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR REGISTRAR in Anæsthetics. Post vacant 7th October, 1957. Regional Training Scheme includes facilities for gaining experience in specialist techniques at regional centres for plastic, thoracic and neuro surgery. Possession of F.F.A.R.C.S. desirable. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, Hendon Group Hospital Management Committee, Edgware General Hospital, by 3rd September, 1957.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. RESIDENT OBSTETRIC HOUSE SURGEON for above Hospital. Post vacant 18th September, 1957. 6 months appointment. Recognised for M.R.C.O.G. and pre-registration purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials, to Medical Director of Hospital by 31st August, 1957.

EDGWARE GENERAL HOSPITAL, Edgware, Middlesex. RESIDENT GYNÆCOLOGICAL HOUSE SURGEON for above Hospital. Post vacant 14th September, 1957. 6 months appointment. Recognised for M.R.C.O.G. purposes.

Applications, stating age, qualifications, experience and enclosing copies of up to 3 recent testimonials, to Medical Director of Hospital by 31st August, 1957.

FARNBOROUGH HOSPITAL, Kent. (800 Beds.) Ortho-PÆDIC SENIOR HOUSE OFFICER required for 1 year from 26th September. Recognised for F.R.C.S.

Apply, stating age, qualifications with dates, and experience, and naming 3 referees, to Administrative Officer.

GATESHEAD. QUEEN ELIZABETH HOSPITAL. SPECIAL GYNÆCOLOGICAL UNIT. GATESHEAD AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. A vacancy exists for a SENIOR HOUSE OFFICER in the above Unit. The Unit is actively engaged in clinical gynæcological research and treatment more especially in connection with malignant diseases of the female pelvis. In conjunction with the Newcastle Regional Cancer Organisation it affords ample opportunity for study of both the surgical and radiotherapeutic methods of treatment. In addition the post offers scope for training in the use of exfoliative cytology in relation to gynæcological disorders both malignant and benign.

Applications with the names of 3 referees should be addressed to Mr. STANLEY WAY, F.R.C.O.G., from whom further particulars may be obtained, at the above Hospital. Application should be submitted within 3 weeks of the appearance of this notice.

GLASGOW. HAWKHEAD (MENTAL) HOSPITAL, 510, Crookston-road, GLASGOW, S.W.3. Applications are invited for the post of SENIOR HOUSE OFFICER in Psychiatry (Male or Female. resident or non-resident). The post offers wide experience and training in all aspects of psychiatry (inpatient and outpatient), and all modern methods of treatment are carried out. Recognised for D.P.M.

Applications, together with the names of 2 referees, should be forwarded as soon as possible to Physician-Superintendent at above address.

GLASGOW, E.3. ROBROYSTON HOSPITAL. Junior HOSPITAL MEDICAL OFFICER required. Resident or non-resident. The work carried out consists mainly of tuberculous pulmonary disease, though substantial units exist for skeletal and for urological tuberculosis. A small unit for acute respiratory disease exists and there are also units for non-tuberculous chest diseases and for geriatrics.

Applications in writing should be forwarded immediately to the Physician-Superintendent.

GLASGOW, S.W.1. SOUTHERN GENERAL HOSPITAL. SENIOR HOUSE OFFICER in Surgery. Recognised for F.R.C.S.

Apply immediately to Secretary, Board of Management for Glasgow South-Western Hospitals, 1301, Govan-road, Glasgow, S.W.1, naming 2 referees.

HASTINGS HOSPITAL MANAGEMENT COMMITTEE. Locum RESIDENT MEDICAL OFFICER (general medicine) required for whole-time duties for 4 weeks commencing 7th September, 1957. Remuneration £19 5s. per week. Non-resident.

Apply, giving details of qualifications and experience, to Group Secretary, Hastings Hospital Management Committee, 11, Holmesdale-gardens, Hastings.

HASTINGS. ROYAL EAST SUSSEX HOSPITAL. (150 Beds.) 2 HOUSE SURGEONS (pre-registration posts). 1 for general surgery and E.N.T., required early September. 1 for general surgery and urology, post vacant 7th October, 1957.

Apply, with copies of testimonials, to the Hospital Administrator.

HILLINGDON HOSPITAL, Uxbridge, Middlesex. (621 Beds.) REGISTRAR for Otorhinolaryngology Department. Ample opportunity for practical operative experience. Post recognised for D.L.O. and for F.R.C.S. (England). Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, Uxbridge Group Hospital Management Committee, "The Furze," Pield Heath-road, Uxbridge, Middlesex, by 3rd September, 1957.

HERTFORD COUNTY HOSPITAL. (173 Beds. Hospital situated 21 miles from London.) RESIDENT CASUALTY OFFICER (Senior House Officer grade) with attachment to Pædiatrician and Ophthalmic Consultant. Salary £819 10s. p.a., less £150 p.a. residential emoluments. Recognised under F.R.C.S. regulations. Appointment to commence 21st September, 1957.

Apply, with full details and references, to Group Secretary, Hertford Hospital Management Committee, County Hospital, Hertford, Herts.

HEREFORDSHIRE GROUP. Registrar in General Surgery. Duties mainly at General (154 Beds—71 surgical beds, including fracture and orthopædic) and County Hospitals, Hereford (339 Beds—40 surgical). Recognised for F.R.C.S.

Application forms from Group Secretary, Victoria House, Eign-street, Hereford, to be returned before 30th August, 1957. Candidates may visit hospitals.

HEXHAM, NORTHUMBERLAND. WOOLEY SANA-TORIUM. JUNIOR RESIDENT MEDICAL OFFICER, to commence duty on 1st October, 1957. The grading is Junior Hospital Medical Officer and is suitable for, and preference will be given to, someone who has suffered from tuberculosis. A detached house, as married accommodation, is available.

Applications to the Medical Superintendent.

HALIFAX GENERAL HOSPITAL. Senior House Officer in General Surgery required at above Hospital. Post vacant 1st September.

Applications to the Group Secretary, Halifax Area Hospitals Management Committee, Royal Halifax Infirmary, Halifax.

HALIFAX. NORTHOWRAM HALL HOSPITAL. (108 Beds.) SENIOR HOUSE OFFICER in Chest Diseases required. Post vacant 8th September, 1957. Duties include attendance at busy chest clinic at the Royal Halifax Infirmary and non-tuberculosis chest ward work. This post offers excellent facilities for a study of chest diseases and experience is available with bronchoscopies and bronchograms. Salary £819 10s. p.a., with a deduction of £150 p.a. for board-residence, &c.

Applications to be forwarded to the Group Secretary, Royal Halifax Infirmary, Halifax.

HITCHIN, HERTFORDSHIRE. LISTER HOSPITAL. CASUALTY OFFICER (resident) now required, for duty with Accident Service and as Orthopædic House Surgeon. Recognised as pre-registration post.

Applications, stating age, nationality, qualifications and experience, together with copies of 3 recent testimonials, to Medical Administrator, Lister Hospital as soon as possible.

HUDDERSFIELD ROYAL INFIRMARY. (285 Beds.) HUDDERSFIELD HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON required to commence duty on 14th September, 1957. The post is recognised as a pre-registration appointment and for the F.R.C.S. Salary in accordance with national scale.

Applications, together with copies of 3 recent testimonials, to be addressed to the undersigned as soon as possible.

H. J. JOHNSON, Secretary to the Management Committee.

The Royal Infirmary, Huddersfield.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE SURGEON (recognised for the F.R.C.S. examinations). There are 69 general surgical beds and some supervision is required of 17 gynæcological beds. Salary £819 10s., less emoluments. Post vacant 1st October, 1957.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HULL. KINGSTON GENERAL HOSPITAL. (419 Beds.) HULL A GROUP HOSPITAL MANAGEMENT COMMITTEE. HOUSE SURGEON (pre-registration post), resident, and tenable for 6 months. This post includes gynæcology and general surgery.

Applications, with 2 recent testimonials, to the Hospital Secretary.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street. Locum CASUALTY OFFICER (Senior House Officer grade) required for the month of September, 1957.

Applications should be sent to the Hospital Secretary.

HULL. VICTORIA HOSPITAL FOR SICK CHILDREN, Park-street, HULL. Locum HOUSE SURGEON required from 26th August to 22nd September, inclusive.

Replies to be addressed to the Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL. Anglesea ROAD WING. (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the E.N.T. and Ophthalmic Departments. The post is recognised for pre-registration and for the D.L.O. examination.

Applications, giving full particulars and copies of recent testimonials, to Hospital Secretary.

IPSWICH AND EAST SUFFOLK HOSPITAL. Anglesea ROAD WING. (356 Beds.) Applications are invited for the post of HOUSE SURGEON to the Fracture and Orthopædic Department. Approved pre-registration post.

Applications, with copies of recent testimonials, to the Hospital Secretary.

IRVINE. AYRSHIRE CENTRAL HOSPITAL. Junior HOSPITAL MEDICAL OFFICER vacancy on 1st October, 1957, in the Infectious Diseases Unit of the above Hospital.

Applications, stating age, qualifications, experience, and giving the names of 2 referees, to the Consultant Physician, Infectious Diseases Unit, Ayrshire Central Hospital, Irvine.

ISLE OF MAN. BALLAMONA HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER at the above Mental Hospital (360 Beds, admission-rate 200 annually), which undertakes all modern methods in the treatment of mental and nervous diseases as well as mental deficiency, and is recognised for training for the Conjoint D.P.M. A choice of 2 furnished flats is available. The terms and conditions of service are those of the Isle of Man Health Service the same as those of the National Health Service. Superannuation is transferable. The Hospital may be visited by appointment.

Those interested should write for further details; and applications, stating age, nationality, qualifications and experience, together with the names of 2 referees, should be sent to the Medical Superintendent.

ISLEWORTH. WEST MIDDLESEX HOSPITAL. North WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR (whole-time) in Obstetrics and Gynecology. 1 year in first instance. Hospital may be visited by direct appointment. Post vacant 1st October, 1957.

Application forms obtainable from, and returnable to, Group Secretary, West Middlesex Hospital, Isleworth, by 31st August.

IVYBRIDGE, SOUTH DEVON. MOORHAVEN HOS-PITAL. SOUTH-WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER. There are 750 Beds and a medical staff of 9. Admissions in 1956 numbered 743 and there were 4674 outpatient attendances at the South Devon and East Cornwall Hospital, Plymouth, and Child Guidance Clinic. The post is a trainee one and secondment with pay to a Part 2 D.P.M. course can be arranged. A good maisonette, suitable for a married man with children, is available at a low rent.

Application form and 1956 Annual Report from the Physician-Superintendent.

KETTERING AND DISTRICT HOSPITAL MANAGE-MENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER to the Geriatric Unit in this area. There are 160 active geriatric beds in the Unit in 3 hospitals. Post vacant 1st September, 1957. Residential accommodation available. National scale of salary.

Applications, together with the names and addresses of 2 referees, to the Group Secretary, Central Administration Offices, General Hospital, Kettering.

KETTERING GENERAL HOSPITAL, Kettering. (130 Beds.) KETTERING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from registered medical practitioners for the appointment of SENIOR HOUSE OFFICER in Anæsthetics. Post vacant now. Post recognised for D.A.

Applications, giving details of qualifications and experience, and enclosing copies of 3 recent testimonials, to be sent to the Group Secretary at the above address.

KING'S LYNN. WEST NORFOLK AND KING'S LYNN GENERAL HOSPITAL. (146 Beds.) KING'S LYNN AREA HOSPITALS MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT HOUSE SURGEON (general surgery) (post recognised for pre-registration), at the above Hospital. Appointment will be for 6 months in the first instance. Post vacant end of August. 8 residents employed.

Applications, with names and addresses of 2 referees, to be forwarded immediately to the Group Secretary of the above Committee, c/o St. James' Hospital, Exton's-road, King's Lynn, Norfolk.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston UPON THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of SENIOR HOUSE OFFICER (E.N.T.). The post which is recognised for D.L.O. purposes includes a small amount of relief duties in the Casualty Department and is available on 22nd September, 1957. Resident or duty-room basis.

Applications, stating age, qualifications and experience, with 2 recent testimonials, should reach the Physician-Superintendent within 10 days of the appearance of this advertisement.

KINGSTON HOSPITAL, Wolverton-avenue, Kingston UPON THAMES. KINGSTON GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited from suitably qualified medical officers for the post of Locum SENIOR HOUSE OFFICER (orthopædic and casualty) for the period 2nd–8th September, 1957.

Applications, stating age, qualifications and experience, with 2 testimonials, should reach the Physician-Superintendent as soon as possible.

LEEDS, 7. CHAPEL ALLERTON HOSPITAL. (229 Beds.) SENIOR HOUSE OFFICER (medical) required. National Health Service terms and conditions.

Apply Medical Superintendent.

LEEDS REGIONAL HOSPITAL BOARD in association with the University of Leeds invites applications for the post of RESEARCH REGISTRAR in Rheumatism to assist the Professor of Clinical Medicine with research projects at the Royal Bath Hospital, Harrogate, which is the centre for the Regional Rheumatism Scheme, or elsewhere in the Region.

Applications, stating age, sex, qualifications, and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary to the Joint Registrars Committee, Park-parade, Harrogate, not later than 5th September, 1957.

LEEDS REGIONAL HOSPITAL BOARD. Registrar vacancies.

Chest Diseases

Scotton Banks Sanatorium, Knaresborough (200 staffed beds). Visiting staff includes Teaching Hospital Consultants. Resident.

General Medicine

St. Luke's Hospital, Bradford (170 general medical beds). Non-resident.

Infectious Diseases

Leeds Road Hospital, Bradford (160 infectious diseases beds). Resident.

Ophthalmology

Huddersfield Group (23 eye beds and 1500 new outpatients annually). Non-resident.

Applications, stating age, qualifications and details of present and previous appointments with dates, together with the names and addresses of 3 referees, to the Secretary, Joint Registrars Committee, Park-parade, Harrogate, by 5th September, 1957.

LEEDS. THE UNITED LEEDS HOSPITALS. The GENERAL INFIRMARY AT LEEDS. SENIOR HOUSE OFFICER in E.N.T. Department required for a period of 6 months. Post vacant mid-September. Terms and conditions of service for hospital medical staff apply.

Applications, giving details of age, qualifications, posts held with dates, and 3 names for reference, should be sent to the Secretary to the Board as soon as possible.

LUTON AND DUNSTABLE HOSPITAL, Luton, Bedford-SHIRE. Locum ANÆSTHETIC REGISTRAR required from 16th September, 1957, until permanent appointment is made.

Applications, giving full particulars and names of referees, to Secretary, Luton and Dunstable Hospital, Luton, Beds.

LUTON AND DUNSTABLE HOSPITAL (250 Beds), AND ASSOCIATED UNITS (134 Beds). NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR (resident or non-resident) required at the above Hospital, for a 1-year or 2-year appointment. Post recognised for D.A. and F.F.A.R.C.S., and vacant 16th September. The Hospital may be visited by direct appointment.

Application forms obtainable from the Secretary, Luton and Hitchin Group Hospital Management Committee, St. Mary's Hospital, Luton, and returnable by 14th September, 1957.

LEICESTER ROYAL INFIRMARY AND LEICESTER GENERAL HOSPITAL. SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time NON-RESIDENT REGISTRAR (dermatology) required with duties at the above Hospitals. Appointment for 1 year in the first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 2nd September, 1957, giving age, nationality, qualifications, present and previous appointments with dates, naming 3 referees.

LEICESTER. TOWERS MENTAL HOSPITAL. (1168 Beds.) Applications are invited for the whole-time post of JUNIOR HOSPITAL MEDICAL OFFICER. Salary £852 10s.–£55–£1182 10s. There is ample opportunity for experience in all branches of psychiatry, including outpatient work and the Hospital is recognised for D.P.M. experience. Facilities for postgraduate training exist at Sheffield University. Resident accommodation is not available. Candidates must have completed their service with H.M. Forces.

Applications, giving age, nationality, and full details with the names of 2 referees, to be sent to the Medical Superintendent as soon as possible.

LINCOLN COUNTY HOSPITAL. (200 Beds.) Applications are invited from pre-registration candidates for appointments as HOUSE SURGEONS for 6 months to be followed if satisfactory by appointments as House Physicians for a further 6 months.

Full particulars should be sent to—

R. W. HOWICK, Group Secretary.

LINCOLN. ST. GEORGE'S HOSPITAL. (121 Beds increasing to 242 in near future.) SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT ANÆSTHETIC REGISTRAR required. Single accommodation available. Duties at other hospitals in the Group if required. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 2nd September, 1957, giving age, nationality, present and previous appointments with dates, naming 3 referees.

LINCOLN. ST. GEORGE'S HOSPITAL. (242 Beds. SHEFFIELD REGIONAL HOSPITAL BOARD. Whole-time RESIDENT REGISTRAR (general medicine) required. Single accommodation available. Appointment for 1 year in first instance.

Apply to Secretary, Sheffield Regional Hospital Board, Old Fulwood-road, Sheffield, by 2nd September, 1957, giving age, nationality, present and previous appointments with dates, naming 3 referees.

LIVERPOOL, 6. NEWSHAM GENERAL HOSPITAL. (1300 Beds.) Applications are invited for the appointment of HOUSE PHYSICIAN to the tuberculosis wards with some duties in general medicine, vacant from 1st October, next. Junior Hospital Medical Officer or Senior House Officer grading according to qualifications and experience. Resident or non-resident. Salary: Junior Hospital Medical Officer £852 10s.–£55–£1182 10s. p.a., Senior House Officer £819 10s. p.a. Resident charges: Junior Hospital Medical Officer £170 p.a. Senior House Officer £150 p.a.

Applications to the Physician-Superintendent at the Hospital as soon as possible. H. BLYTHE, Group Secretary.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ST. PAUL'S EYE HOSPITAL. Applications are invited for a Locum appointment as SENIOR REGISTRAR in Ophthalmology for a period of about 2 months from 9th September.

Apply immediately on form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

LIVERPOOL. THE UNITED LIVERPOOL HOSPITALS. ROYAL LIVERPOOL CHILDREN'S HOSPITAL. Applications are invited for a post of HOUSE SURGEON at the Heswall Branch of the Royal Liverpool Children's Hospital for the period 1st September, 1957–28th February, 1958. The post is open to both pre-registration and post-registration candidates.

Apply immediately for an application form obtainable from the Secretary, 80, Rodney-street, Liverpool, 1.

MACCLESFIELD AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. HOUSE OFFICER in Surgery (pre-registration post). Acute Surgical Unit of 100 Beds. Recognised for F.R.C.S. purposes. Main casualty duties undertaken by Senior Resident Practitioner.

Apply immediately to Group Secretary, "Willerby House," Cumberland-street, Macclesfield.

MAIDSTONE. PRESTON HALL HOSPITAL, British LEGION VILLAGE, MAIDSTONE, KENT. Applications are invited for the post of SENIOR HOUSE OFFICER at the above Hospital, which contains 330 Beds for treatment of pulmonary tuberculosis and other chest diseases and includes a major Thoracic Surgical Unit. Candidates should have had experience in general medicine and in the treatment of pulmonary tuberculosis in adults. Salary £819 10s. p.a., national scale and conditions.

Applications, stating age, qualifications and experience, with relevant dates, together with names and addresses of 2 referees, to be sent to the Group Secretary, by 21st September, 1957.

MANCHESTER. WEST MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. PARK HOSPITAL, DAVYHULME. (General Hospital—433 Beds.) JUNIOR HOUSE OFFICER (pædiatrics) required, mid-August. Post-registration. There is a Midwifery Unit of 73 Beds and a Pædiatric Unit which includes 10 thoracic surgical beds. Recognised for D.C.H.

Application forms from Secretary.

MANCHESTER. DUCHESS OF YORK HOSPITAL FOR BABIES, MANCHESTER, 19, AND WYTHENSHAWE HOSPITAL. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics) vacant 1st October. A joint post of not less than 3 months and preferably 6 months at each Hospital is recognised as training for the D.C.H.

Applications, with full details and the names of 2 referees, to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER. BOOTH HALL CHILDREN'S HOSPITAL, BLACKLEY, MANCHESTER, 9. (380 Beds. Recognised for D.C.H.)

RESIDENT SENIOR HOUSE OFFICER (surgical).

Applications, giving names and addresses of 2 referees, to be sent to Group Secretary, from whom further particulars may be obtained.

HOUSE OFFICER (surgical), pre- or post-registration. Duties mainly general surgery and neuro-surgery. Post vacant 8th October.

Applications, with usual particulars and copies of 2 recent testimonials, to Group Secretary.

MANCHESTER. CRUMPSALL HOSPITAL. North MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of REGISTRAR in the Department of Neurosurgery at the above Hospital. A new department of over 20 Beds, for adult cases, is being started and will become self-contained unit. Facilities will be made available for the successful applicant to gain experience in psychosurgery at neighbouring hospitals, and if desired, pædiatric surgery.

Applications, with names of 2 referees, by 14th September, 1957, to Group Secretary, Crumpsall Hospital, Manchester.

MANCHESTER REGIONAL HOSPITAL BOARD. Blackburn ROYAL INFIRMARY. REGISTRAR (medicine) required early September, 1957. Resident post. Duties at Royal Infirmary Blackburn (262 acute beds), as arranged by Consultant Physician.

Application forms from Group Secretary, Hospital Management Committee Office, Royal Infirmary, Blackburn, Lancs.

MANCHESTER REGIONAL HOSPITAL BOARD. Hope HOSPITAL, SALFORD. SALFORD HOSPITAL MANAGEMENT COMMITTEE. ORTHOPÆDIC REGISTRAR, required mid-September, 60 adult and children's beds. Duties also at Salford Royal and Royal Manchester Children's Hospitals.

Applications to Group Secretary, Salford Royal Hospital, Salford, 3, before 30th August, 1957.

MANCHESTER. SOUTH MANCHESTER HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR HOUSE OFFICER (anæsthetics) with duties in the South Manchester Group. This post is recognised by the Royal College of Surgeons for the F.F.A.R.C.S. and for the D.A.

Applications, stating age, present post, experience, and the names of 2 referees, to be forwarded immediately to the Group Secretary, Withington Hospital, Manchester, 20.

MANCHESTER (near). PRESTWICH HOSPITAL. (3042 Beds.) REGISTRAR in Psychiatry required at above Hospital. Residential accommodation available for single person. All modern treatments practised and facilities granted for study for the D.P.M.

Applications, giving full details of age, training and experience, with the names and addresses of at least 2 referees, should be sent to the Medical Superintendent, Prestwich Hospital, P.O. Box No. 1, Prestwich, near Manchester, not later than Saturday, 31st August, 1957.

MONTROSE, ANGUS, SCOTLAND. ROYAL MENTAL HOSPITAL. (944 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (Male or Female). A self-contained, furnished house is available for a married man. Single furnished quarters are also available. All subject to appropriate deductions. Previous experience in psychiatry is not essential. Salary and conditions of service in accordance with national scale.

Applications, stating age, qualifications and experience, together with the names and addresses of 2 referees, should be forwarded immediately to the Physician-Superintendent.

NEWTON ABBOT HOSPITAL, S. Devon. Senior House OFFICER (medicine), Male or Female, required approximately 1st October, 1957. Duties divided equally between 20 acute medical beds in General Section and 140 geriatric beds. This Officer is also required to stand in when Senior House Surgeon otherwise engaged. Married quarters available.

Applications, stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

NEWTON ABBOT HOSPITAL. (General Section—65 Beds.) RESIDENT SENIOR HOUSE SURGEON (Male or Female), required mid-September, 1957. Married quarters available.

Applications (quoting Ref. F.364/39), stating qualifications, nationality, age, with copy testimonials, to be sent to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

NEWCASTLE REGIONAL HOSPITAL BOARD.

2 REGISTRAR PSYCHIATRISTS (whole-time) for the Department of Psychological Medicine, Newcastle General Hospital. The department is associated with the University Department of Psychological Medicine under the general direction of the Professor of Psychiatry, and contains an active Child Guidance Unit. The appointees will be able to take the Durham University D.P.M. course. Single accommodation available. Married person may be non-resident by arrangement.

2 Locum Tenens REGISTRAR PSYCHIATRISTS (whole-time) for the Department of Psychological Medicine, Newcastle General Hospital, for a period of approximately 6 months from 1st October, 1957. Single accommodation available. Married person may live out by arrangement.

Applications, with names and addresses of 2 referees, to the Regional Psychiatrist, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Senior REGISTRAR PATHOLOGIST (whole-time), non-resident, East Cumberland Group of hospitals—main hospital, Cumberland Infirmary, Carlisle (332 Beds).

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE REGIONAL HOSPITAL BOARD. Registrar ANÆSTHETIST (whole-time), Tees-side Group of hospitals—main hospital, North Ormesby (184 Beds). Resident, or non-resident near main hospital. Male single accommodation available. Post recognised for F.F.A.R.C.S. examination.

Applications, with names and addresses of 3 referees, to Senior Administrative Medical Officer, Regional Hospital Board, Benfield-road, Newcastle upon Tyne, 6, within 14 days.

NEWCASTLE GENERAL HOSPITAL. (838 Beds.) NEWCASTLE UPON TYNE HOSPITAL MANAGEMENT COMMITTEE. SENIOR HOUSE OFFICER (Accident and Admission Department). Post vacant 31st August, 1957. Recognised for F.R.C.S.

Applications, with names and addresses of 2 referees, should be forwarded to the Secretary, Newcastle General Hospital, Westgate-road, Newcastle upon Tyne, 4, as soon as possible.

NEWCASTLE. THE UNITED NEWCASTLE UPON TYNE HOSPITALS. ROYAL VICTORIA INFIRMARY. Applications are invited for the whole-time non-resident appointment of REGISTRAR in the Orthopædic Department at the Royal Victoria Infirmary. The successful candidate will be required to teach in his subject and preference will be given to applicants who have passed the Primary Fellowship examination. The appointment is for 1 year in the first instance and will be subject to the terms and conditions of service of hospital medical staff in the National Health Service.

Applications, giving full details and the names and addresses of 3 referees, should be sent to the undersigned within 2 weeks of the appearance of this advertisement.

A. W. SANDERSON, House Governor and Secretary.

Royal Victoria Infirmary, Newcastle upon Tyne, 1.

NEWPORT, MONMOUTHSHIRE. ROYAL GWENT HOSPITAL. (260 Beds. 10 Residents. Recognised F.R.C.S.) SENIOR HOUSE OFFICER required for Casualty Department which is under the full-time charge of a Senior Hospital Medical Officer and there are also 2 Senior House Officers. The Department has recently been rebuilt and re-equipped, and all medical and surgical emergency admissions pass through it. Tenable for 6 or 12 months at candidate's option. Excellent experience.

Write, quoting 2 referees, to T. A. JONES, Group Secretary. 64, Cardiff-road, Newport, Mon.

NORTHAMPTON GENERAL HOSPITAL. (482 Beds.) Vacancies 1st October, 1957, for the following :—

HOUSE OFFICER (general surgery). Recognised for F.R.C.S.

HOUSE OFFICER (Fracture and Orthopædic Department). Recognised for F.R.C.S.

HOUSE OFFICER (Department of Anæsthetics). Recognised for D.A.

SENIOR HOUSE OFFICER (general surgery), with some duties at Northampton General Hospital but mostly for General Surgical Unit at Manfield Orthopædic Hospital.

Posts of House Officer General Surgery and House Officer Fracture and Orthopædic Department recognised for pre-registration. 6 months appointments in first instance.

Applications as soon as possible to S. G. HILL, Superintendent.

NORTHAMPTON (near). CREATON HOSPITAL. (138 Beds.) Applications are invited for the posts of SENIOR HOUSE OFFICER and HOUSE OFFICER. The House Officer post is recognised as a pre-registration medical appointment. The Hospital is for the treatment of both pulmonary and non-pulmonary tuberculosis. There is a modern major Thoracic Surgical Unit for tuberculous and non-tuberculous diseases of the chest.

Applications, stating age, experience and qualifications, together with the names and addresses of 2 referees, should be sent to the Secretary, Northampton and District Hospital Management Committee, General Hospital, Northampton.

NORTHWOOD, MIDDLESEX. MOUNT VERNON HOS-PITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. ANÆSTHETIC REGISTRAR (resident) required for 1 year in first instance. This post is recognised for F.F.A.R.C.S. examination.

Application forms obtainable from, and returnable to, the Group Secretary, Harefield and Northwood Group Hospital Management Committee, Mount Vernon Hospital, Northwood, Middlesex, by 31st August, 1957.

NOTTINGHAM GENERAL HOSPITAL. A Senior HOUSE OFFICER (orthopædic and fracture) required 30th September. Post offers exceptional experience in traumatic surgery.

Applications, stating age, qualifications, experience, nationality together with copies of testimonials, to be sent to Group Secretary.

NOTTINGHAM CHILDREN'S HOSPITAL. (136 Beds. Recognised for the D.C.H.) Applications are invited for the post of SENIOR HOUSE OFFICER (surgical) which will be vacant mid-September. The post is tenable for 6 months or a year by agreement.

Applications, with the copies of 2 testimonials, should be sent to the Secretary, Nottingham Children's Hospital, Chestnut-grove, Nottingham.

NOTTINGHAM. CITY HOSPITAL. (811 Beds.) Applica-tions are invited for the post of HOUSE OFFICER (obstetrics and gynæcology), recognised for pre-registration purposes which will be graded Senior House Officer or House Officer in accordance with experience. Recognised for the M.R.C.O.G. and D.Obst.R.C.O.G. Post vacant on 6th October, 1957.

Applications, stating age, nationality, qualifications, and experience, together with copies of not more than 3 testimonials, to be sent to the Hospital Secretary, City Hospital, Hucknall-road, Nottingham.

OXFORD REGIONAL HOSPITAL BOARD. Registrar in General Medicine to the Northampton General and Associated Hospitals. The post will be for 1 year and be eligible for extension to a second year.

Applications, on forms obtainable from the Secretary, Registrar Committee, 43, Banbury-road, Oxford, should reach him by 30th August.

OXFORD. UNITED OXFORD HOSPITALS: OXFORD REGIONAL HOSPITAL BOARD. FIRST ASSISTANT (Senior Registrar) to the Accident Service in the United Oxford Hospitals, interchangeable with an orthopædic post in the Nuffield Orthopædic Centre, Oxford. The period of tenure will be approximately equally divided between the 2 posts, and the successful candidate may be required to start in either. Candidates should be Fellows of 1 of the Royal Colleges of Surgeons. Experience in both branches of orthopædics is essential.

Applications, on forms obtainable from the Secretary, Joint Committee for Senior Registrars, 43, Banbury-road, Oxford, should reach him by 31st August.

OXFORD. UNITED OXFORD HOSPITALS. Applications are invited for 3 posts of NON-RESIDENT REGISTRAR in the Department of Anæsthetics, with effect from 1st November, 1st December, 1957, and 1st January, 1958, for 1 year in the first instance, eligible to an extension for a second year.

Applications, on forms obtainable from the Administrator, Radcliffe Infirmary, Oxford, should be received not later than 7th September, 1957.

OXFORD. UNITED OXFORD HOSPITALS. Applications are invited for the post of RESIDENT JUNIOR PATHOLOGIST for 6 months at the Radcliffe Infirmary, Oxford. The post is graded at Senior House Officer rate, £819 10s. p.a., and will be vacant with effect from 1st October, 1957.

Applications, stating age, qualifications and experience, together with the names of 2 referees, to the Administrator, Radcliffe Infirmary, Oxford, as soon as possible.

OSWESTRY. THE ROBERT JONES AND AGNES HUNT ORTHOPÆDIC HOSPITAL. SENIOR SURGICAL HOUSE OFFICER (resident) required.

Apply Secretary immediately.

PETERBOROUGH. THE MEMORIAL HOSPITAL. PETERBOROUGH AND STAMFORD HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the position of HOUSE SURGEON, now vacant.

Applications, with testimonials, should be addressed to the Secretary, Memorial Hospital, Peterborough.

PORTSMOUTH GROUP HOSPITAL MANAGEMENT COMMITTEE. QUEEN ALEXANDRA HOSPITAL. (78 medical beds.) HOUSE PHYSICIAN (pre-registration), vacant 15th September.

Applications, stating age, experience and qualifications, together with the names of 2 referees, should be forwarded as soon as possible to E. H. HURST.

Saint Mary's Hospital, Milton-road, Portsmouth.

READING AND DISTRICT HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of RESIDENT SENIOR HOUSE OFFICER (area Accident and Orthopædic Department), vacant immediately. Recognised for F.R.C.S. Duties including work in area Casualty Department at Battle Hospital, Reading, (300 Beds). Person appointed will work with Registrar and House Officers.

Apply, stating nationality, present post, and qualifications with dates, together with names of 2 referees, to Group Secretary, 3, Craven-road, Reading.

REDHILL COUNTY HOSPITAL, Earlswood Common, REDHILL, SURREY. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR in Clinical Pathology for appointment to Group Laboratory. Post expected to become vacant 30th November, 1957. Visits by arrangement with Group Pathologist, telephone Redhill 3581.

Application forms from Group Secretary, above address.

ROCHFORD, ESSEX. GENERAL HOSPITAL. (622 Beds.) HOUSE PHYSICIAN (pre-registration) required, vacant 14th September, 1957.

Applications, &c. (1 testimonial only necessary for pre-registration applicant seeking first appointment), to be sent to the undersigned by 26th August, 1957. J. C. FIELD, Secretary.

ROMFORD, ESSEX. VICTORIA HOSPITAL. (99 Beds.) RESIDENT HOUSE SURGEON (Male) required immediately. (Not pre-registration appointment.)

Applications should be forwarded to the Secretary, Romford Group Hospital Management Committee, Oldchurch Hospital, Romford.

SALISBURY GENERAL HOSPITAL. Salisbury Group HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of SENIOR RESIDENT HOUSE SURGEON or RESIDENT HOUSE SURGEON which is now vacant. The appointment is also recognised for pre-registration candidates. The Department has over 50 Beds and a large outpatient turnover, dealing with fractures and all types of orthopædic surgery.

Applications, stating age, nationality, qualifications and experience, and naming 2 referees, to the Group Secretary, Odstock Hospital, Salisbury.

SALISBURY GENERAL HOSPITAL. South West Metro-POLITAN REGIONAL HOSPITAL BOARD. SALISBURY GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for the post of REGISTRAR ANÆSTHETIST (resident or non-resident) at above Hospital, which is recognised for the F.F.A.R.C.S.

Further details and application forms obtainable from, and should be returned to, Group Secretary, Odstock Hospital, Salisbury, Wiltshire, within 10 days of the appearance of this advertisement.

SHREWSBURY. ROYAL SALOP INFIRMARY/COP-THORNE HOSPITAL. (500 Beds.) SHREWSBURY HOSPITAL GROUP. HOUSE SURGEON, vacant 1st November, 1957. Pre-registration candidates eligible. Recognised for the F.R.C.S.

Applications with copy testimonials, to Group Secretary, Royal Salop Infirmary, Shrewsbury.

SHREWSBURY. ROYAL SALOP INFIRMARY AND COPTHORNE HOSPITAL. (500 Beds.) RESIDENT ANÆSTHETIST (Senior House Officer). Post recognised for F.F.A.R.C.S. Registrar also employed. Vacant mid-September.

Applications and copy testimonials to Group Secretary, Shrewsbury Hospital Group, Royal Salop Infirmary, Shrewsbury.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD invites applications for the post of Whole-time NON-RESIDENT JUNIOR HOSPITAL MEDICAL OFFICER at Inverness. The post provides experience in general practice as Locum Tenens as well as hospital work in selected departments. Tenure of appointment is 1 year.

A note of further particulars and an application form are obtainable from the undersigned, with whom applications should be lodged by 7th September, 1957.

A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

SCOTLAND. NORTHERN REGIONAL HOSPITAL BOARD. Applications are invited for the whole-time post of REGISTRAR in Anæsthetics. Duties mainly at the Royal Northern Infirmary, Inverness, and Raigmore Hospital, Inverness.

Forms of application and further particulars may be obtained from the undersigned, with whom applications should be lodged by 9th September, 1957. A. M. FRASER, M.D.,
Secretary and Administrative Medical Officer.
Office of the Northern Regional Hospital Board,
Raigmore, Inverness.

SCOTLAND. EASTERN REGIONAL HOSPITAL BOARD. General Surgery. DUNDEE TEACHING HOSPITALS. Applications are invited for a post as REGISTRAR attached to the Dundee Teaching Hospitals (Dundee Royal Infirmary, 534 Beds, and Maryfield Hospital 370 Beds). Applicants should have had previous experience in general surgery and have passed at least a Primary Fellowship examination. Salary and conditions in accordance with national agreement.

Further particulars and forms of application may be obtained from the Secretary to the Board, 430, Blackness-road, Dundee, with whom applications must be lodged not later than 31st August, 1957.

SCOTLAND. NORTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR or SENIOR REGISTRAR in Dermatology at the Aberdeen Royal Infirmary. The appointment will be filled in either of these grades according to the experience and qualifications of the applicant. Opportunity will be given for further study and training in general medical subjects by arrangement with the Department of Medicine.

Applications, giving the names of 2 referees, should be submitted by 6th September, 1957, to the Secretary, North-Eastern Regional Hospital Board, Scotland, 1, Albyn-place, Aberdeen, from whom further particulars may be obtained.

SCOTLAND. SOUTH-EASTERN REGIONAL HOSPITAL BOARD. Applications are invited from suitably qualified persons for the post of MEDICAL OFFICER on the Board's Headquarters staff at a salary of £1415 (at age 33 or over)–50(4)–65(1)–£1680 p.a. The successful applicant will be required to undertake duties under the direction of the Senior Administrative Medical Officer in the medical administration of the hospital and specialist services of the Region. The appointment will be whole-time and subject to the approved Whitley Council Conditions.

Applications, stating age, qualifications, and details of present and previous appointments with dates, and names and addresses of 3 referees, to the Secretary, 11, Drumsheugh-gardens, Edinburgh, by 21st September, 1957.

SCOTLAND. WESTERN REGIONAL HOSPITAL BOARD. Applications are invited for the following appointments, which will be for 1 year in the first instance :—

SENIOR REGISTRAR in Radiotherapy based at the Western Infirmary, Glasgow.

REGISTRAR in Surgery based at the Western Infirmary, Glasgow, with duties for a period at the Lewis Hospital, Stornoway.

REGISTRAR in Surgery based at the Royal Infirmary, Glasgow.

REGISTRAR in Surgery based at Broadstone Hospital, Port Glasgow. A house is available.

REGISTRAR in Radiodiagnosis based at the Victoria Infirmary, Glasgow.

REGISTRAR in Medicine based at Stobhill General Hospital, Glasgow.

REGISTRAR in Medicine based at the Royal Alexandra Infirmary, Paisley.

Applications (12 copies), stating date of birth, qualifications, experience, present appointment, and the names of 3 referees, to reach the Secretary, Western Regional Hospital Board, 64, West Regent-street, Glasgow, C.2, by 7th September, 1957.

SHOTLEY BRIDGE GENERAL HOSPITAL, Shotley BRIDGE, CONSETT, CO. DURHAM. REGIONAL THORACIC UNIT (150 Beds. Mainly non-tuberculous.) RESIDENT MEDICAL OFFICER (House Officer or Senior House Officer grading) required as soon as possible. Work concerned with the pre- and post-operative management and investigation of pulmonary, cardiovascular and œsophageal cases but duties include some surgical work.

Applications, stating age, qualifications, experience, and enclosing copies of 2 recent testimonials, to the Group Secretary.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Obstetrics and Gynæcology to fill a vacancy in the approved trainee establishment at the Bromley Group of hospitals, available on 1st November, 1957. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, 11, Portland-place, W.1, not later than 7th September, 1957.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for a whole-time appointment as ANÆSTHETIST (second year Registrar) to fill a vacancy in the approved establishment at Eastbourne Group of hospitals. The salary will be £1061 10s. p.a. and the appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance, renewable for a further year.

Applications, giving particulars of age, qualifications and experience with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, W.1, not later than 7th September, 1957.

SOUTH EAST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for an appointment as Whole-time REGISTRAR in Anæsthetics to fill a vacancy in the approved trainee establishment at the Medway and Gravesend Group of hospitals. Duties will be at St. Bartholomew's Hospital, Rochester, All Saints Hospital, Chatham, and the Gravesend and North Kent Hospital, Gravesend, all of which are recognised for the F.F.A.R.C.S. The appointment will be in accordance with the terms and conditions of service of hospital medical and dental staffs (England and Wales), and will be for 1 year in the first instance.

Applications, giving particulars of age, qualifications and experience, with relevant dates, together with the names and addresses of 2 referees, to be sent to the Secretary, Registrars Committee, South East Metropolitan Regional Hospital Board, 11, Portland-place, London, W.1, not later than 7th September, 1957.

SOUTHAMPTON CHEST HOSPITAL. South West METROPOLITAN REGIONAL HOSPITAL BOARD. SENIOR SURGICAL REGISTRAR (Dominions status) required for Thoracic Unit (80 surgical beds) at above Hospital. Candidates should possess higher qualifications and should have had previous experience of thoracic surgery. This post will be for a maximum of 2 years and is intended for candidates from overseas (particularly from the Commonwealth), who are already of Senior Registrar status who wish to undertake a period of final training here before returning to their own country. The Hospital may be visited, if desired, by prior arrangement.

Application forms, obtainable from the undersigned, should be returned by 4th September, 1957.

FRANK JENNINGS, Group Secretary,
Southampton Group Hospital Management Committee.
Bullar-street, Southampton.

SOUTHAMPTON CHEST HOSPITAL. (252 Beds.) SENIOR HOUSE OFFICER required, to be responsible for Infectious Diseases Unit. The duties are such as to suit a candidate reading for higher examinations. The Unit is sited at a Hospital possessing up-to-date Tuberculosis and Thoracic Surgical Units, whilst the Southampton Group of hospitals, as a whole affords excellent opportunities for study and experience in all branches of medicine.

Applications, together with copies of recent testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON GENERAL HOSPITAL. (474 Beds. Recognised for the Membership and Diploma Examinations of the R.C.O.G.) RESIDENT HOUSE SURGEON to the Gynæcological and Obstetric Unit required beginning October.

Applications, with copies of recent testimonials, should be forwarded as soon as possible to the Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. †274 Beds.) RESIDENT HOUSE SURGEON required beginning of October. Pre-registration candidates eligible.

Applications, with copies of recent testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton.

SOUTHAMPTON. ROYAL SOUTH HANTS HOSPITAL. (274 Beds.) RESIDENT HOUSE PHYSICIAN required mid-September. Pre-registration candidates eligible.

Applications, with copies of testimonials, should be forwarded to Group Secretary, Southampton Group Hospital Management Committee, Bullar-street, Southampton, as soon as possible.

SOUTHEND GENERAL HOSPITAL. Applications are invited from registered or provisionally registered practitioners for the post of RESIDENT HOUSE SURGEON, vacant 9th September, 1957.

Applications, stating age, qualifications, &c. (1 testimonial sufficient from pre-registration candidates seeking first appointment), to reach the undersigned as soon as possible.

J. C. FIELD, Secretary.

SOUTHEND-ON-SEA GENERAL HOSPITAL. Locum MEDICAL REGISTRAR (resident or non-resident) required for 9th–28th September, 1957, inclusive.

Applications, giving details of age, qualifications, testimonials, &c., to be sent to the undersigned as soon as possible.

J. C. FIELD, Secretary.

SHEFFIELD. NETHER EDGE HOSPITAL. Applications are invited for the resident post of SENIOR HOUSE OFFICER. Main duties will be in connection with the Maternity Unit but will also be required to assist in the wards for long-stay medical cases. Small flat available on rental.

Apply, giving full details of age, qualifications, present and previous appointments with dates, and the names of 2 persons for reference, to the Group Secretary, Nether Edge Hospital, Sheffield, 11.

STIRLING AND CLACKMANNAN HOSPITALS BOARD OF MANAGEMENT. There is a vacancy for a HOUSE PHYSICIAN at Stirling Royal Infirmary for the period up to 31st January, 1958.

Applications should be sent to the Group Medical Superintendent, Royal Infirmary, Stirling.

SLOUGH, BUCKINGHAMSHIRE. UPTON HOSPITAL. Locum SENIOR SURGICAL REGISTRAR required 2nd–15th September.

Applications, with names of 2 referees, to Secretary.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. HOUSE OFFICER (pædiatrics) required, vacant very shortly. Pre-registration post.

Detailed applications, with copy testimonials, to Group Secretary, Princes-road, Stoke-on-Trent.

STOKE-ON-TRENT. CITY GENERAL HOSPITAL. (815 Beds.) HOUSE OFFICER (general surgery) required, vacant end August. Pre-registration post. Hospital recognised for F.R.C.S.

Detailed applications, with copy testimonials, to Group Secretary, Hospital Management Committee, Princes-road, Stoke-on-Trent.

STOCKPORT INFIRMARY. (163 Beds.) Locum Senior HOUSE OFFICER (Casualty Officer) required from 6th September.

Applications, with full particulars, and copies of 2 recent testimonials, to the Secretary, Stockport and Buxton Hospital Management Committee, 59B, Shaw-heath, Stockport.

ST. ALBANS (near), HERTFORDSHIRE. SHENLEY HOSPITAL. (2360 Beds.) Applications are invited for the post of JUNIOR HOSPITAL MEDICAL OFFICER (psychiatry) which offers experience in all branches of psychiatry, including modern forms of treatment. Single accommodation available. The Hospital is 15 miles from London, and may be visited by appointment.

Application forms obtainable from, and returnable to, the Group Secretary by 2nd September.

ST. ALBANS, HERTFORDSHIRE. HARPERBURY HOSPITAL. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required at above Hospital. This is a modern Hospital where 1729 mental defectives of all types and ages are under care. Approved for D.P.M. Hospital may be visited by direct appointment.

Application forms obtainable from, and returnable to, Group Secretary, Harperbury Hospital, St. Albans, Herts.

ST. ALBANS, HERTFORDSHIRE. NAPSBURY MENTAL HOSPITAL. Applications are invited for the post of SENIOR HOUSE OFFICER, appointment to commence immediately. Previous experience as House Physician or House Surgeon essential. Previous psychiatric experience desirable but not essential. Regular clinical case conferences, good psychiatric library and other training facilities. Salary £819 10s. p.a. Residential accommodation is available, if required, for which a charge will be made. No married quarters.

Applications, with references or testimonials, to be sent not later than 3rd September, 1957, to the Medical Superintendent (telephone : Bowmansgreen 2181).

ST. HELENS AND DISTRICT HOSPITAL MANAGE- MENT COMMITTEE. ST. HELENS HOSPITAL. (196 Beds.) Applications are invited for the post of RESIDENT HOUSE SURGEON, which becomes vacant from 1st September, 1957. The post is recognised for Pre-registration Service and for the F.R.C.S. examination.

Applications stating age, date of qualification, and experience, and giving 2 names for reference, should be forwarded to N. RICHARDS, Group Secretary, Whiston Hospital, Prescot, Lancs, immediately.

TAPLOW, near MAIDENHEAD. CANADIAN RED CROSS MEMORIAL HOSPITAL. HOUSE PHYSICIAN required for post vacant 14th September. Pre-registration post.

Applications, stating age, experience and qualifications with dates, with copies of 2 testimonials, to Secretary.

TORQUAY. TORBAY HOSPITAL. Resident Senior HOUSE OFFICER (surgery) required mid-September, 1957. Post recognised for F.R.C.S. There is a complement of 6 Resident House Officers.

Applications, stating qualifications, age, nationality, with copy testimonials (quoting Ref. F.955/83), to the Group Secretary, Torquay District Hospital Management Committee, Torbay Hospital, Torquay, S. Devon.

WEST MALLING, KENT. LEYBOURNE GRANGE COLONY. Required, Locum Tenens JUNIOR HOSPITAL MEDICAL OFFICER immediately. Appointment for 1 month in the first instance. Residential accommodation available.

Applications to Group Secretary as soon as possible.

WATFORD CHEST CLINIC, Peace Memorial Hospital, WATFORD. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications invited for the post of REGISTRAR at the above Clinic and associated beds (tuberculosis 47, chest medicine 16) at Shrodells and Holywell Hospitals. This is a new chest clinic. Experience in general medicine and tuberculosis work, including refill techniques, is essential. This chest unit is closely associated with Harefield Hospital, the Physician-in-charge being on the Consultant staff of this hospital. Applicants invited to visit the clinic and should contact the Physician-in-charge.

Application form obtainable from, and returnable to, the Secretary, West Herts Group Hospital Management Committee, 9, Rickmansworth-road, Watford, Herts, by not later than 10 days after the appearance of this advertisement.

WATFORD. SHRODELLS HOSPITAL. Applications are invited for the post of HOUSE OFFICER (Senior House Officer grade) to the Pædiatric Unit of 38 Beds. Post recognised for the D.C.H. To take up duty at the end of September.

Applications, together with copies of 2 recent testimonials, should reach the Medical Officer-in-charge as soon as possible.

WATFORD, HERTFORDSHIRE. PEACE MEMORIAL HOSPITAL. CASUALTY OFFICER (Senior House Officer). Modern Department employing 3 full-time Casualty Officers. Post recognised for F.R.C.S. Resident or non-resident. Vacant immediately.

Applications, with names of 2 referees, to the Administrator.

WORTHING GROUP HOSPITAL MANAGEMENT COM- MITTEE. Applications are invited for the post of REGISTRAR in Pathology, vacant from end of September, 1957. This is a Group appointment with duties at the 2 main Hospitals : Southlands Hospital (427 Beds) and Worthing Hospital (210 Beds).

Forms of application are available from the undersigned.

A. V. OAKTON, Group Secretary.

129, Brighton-road, Worthing, Sussex.

WELSH REGIONAL HOSPITAL BOARD. Applications are invited for the appointment of SENIOR REGISTRAR in Orthopædic Surgery to the Prince of Wales Orthopædic Hospital, Rhydlafar, Cardiff (Cardiff Hospital Management Committee). This Hospital provides about 330 Beds and is the Regional Orthopædic Centre for the South Wales area. Accommodation for a married man is available. The post will be subject to review annually.

Forms of application should be obtained from the Senior Administrative Medical Officer, Welsh Regional Hospital Board, Cathays Park, Cardiff, within 14 days of appearance of this advertisement.

WELSH REGIONAL HOSPITAL BOARD.

2 REGISTRARS (general surgery), Llanelly. (Resident.)

REGISTRAR (general surgery), Pembroke County War Memorial Hospital, Haverfordwest. (Resident or non-resident.)

REGISTRAR in Thoracic Medicine, Sully Hospital, Sully, near Penarth, Glam. (324 Beds). (Resident or non-resident.) Regional Centre for pulmonary tuberculosis and all other chest and heart conditions.

Subject to review end of first year.

Application forms from Senior Administrative Medical Officer, Temple of Peace, Cathays Park, Cardiff, within 14 days.

WEST DORSET GROUP HOSPITAL MANAGEMENT COMMITTEE. Applications are invited for 2 resident 6-monthly posts of HOUSE PHYSICIAN at :—

(*a*) WEYMOUTH AND DISTRICT HOSPITAL (124 Beds), vacant mid-September.

(*b*) DORSET COUNTY HOSPITAL, DORCHESTER (109 Beds), vacant 1st October.

Both posts are approved for Pre-registration Service.

Applications, stating age, qualifications, experience and nationality, together with copies of testimonials, to the Group Secretary, West Dorset Hospital Management Committee, Damers-road, Dorchester, Dorset, immediately.

WEST HERTS GROUP HOSPITAL MANAGEMENT COMMITTEE. NORTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. REGISTRAR required for Geriatric Units based at Shrodells Hospital, Watford, and St. Paul's Hospital, Hemel Hempstead. Hospitals may be visited by arrangement.

Further details and application form obtainable from, and returnable to, Group Secretary, 9, Rickmansworth-road, Watford, Herts, by not later than 10 days after appearance of this advertisement.

WHITEHAVEN HOSPITAL, Cumberland. (119 Beds. Pre-registration post. Recognised F.R.C.S.(Ed.).) HOUSE SURGEON (first, second or Senior House Officer post), vacant immediately.

Detailed applications, with dates, and names of 2 referees, to Secretary, Workington Infirmary, Cumberland.

WHITEHAVEN HOSPITAL, Cumberland. (119 Beds, plus 31 Beds in Annexe.) HOUSE SURGEON, with orthopædic and casualty duties. Recognised pre-registration, Senior House Officer grade if appropriate. Vacant end of September.

Detailed application, with dates, and names of 2 referees, to Group Secretary, Workington Infirmary, Cumberland.

WIGAN AND LEIGH HOSPITAL MANAGEMENT COMMITTEE.

Royal Albert Edward Infirmary, Wigan

HOUSE SURGEON.

Leigh Infirmary

HOUSE SURGEON.

Both pre-registration posts—becoming vacant shortly.

Applications, with names of 2 referees, to the Secretary, Knowsley House, Wigan.

WINCHESTER GROUP HOSPITAL MANAGEMENT COMMITTEE. SOUTH WEST METROPOLITAN REGIONAL HOSPITAL BOARD. Applications are invited for the post of REGISTRAR in the Department of Pathology, preferably resident. Post vacant 23rd September. The person appointed will work at the main hospital (315 Beds). Work will include all branches of pathology. Post recognised by the Examining Board in England for Diploma in Pathology.

Application forms obtainable from Group Secretary, Royal Hampshire County Hospital, Winchester, to be completed and returned as soon as possible.

WINCHESTER. ROYAL HAMPSHIRE COUNTY HOS- PITAL. (315 Beds.) HOUSE PHYSICIAN (pre-registration), vacant 6th October.

Applications, with copies of 2 testimonials, to the Group Secretary.

WREXHAM. WAR MEMORIAL HOSPITAL. (230 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER in the Orthopædic Department of the above Hospital. The post is a residential one and affords particular facilities for postgraduate study. Successful applicant will be allowed to attend for 2 days a month at the Robert Jones and Agnes Hunt Orthopædic Hospital, Oswestry. The Hospital is recognised for the Diploma of F.R.C.S. (Eng. and Edin.).

Applications, stating age, nationality, qualifications, and experience, together with copies of 2 recent testimonials, to be addressed to the Group Secretary, Maelor General Hospital, Wrexham, as soon as possible.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (634 Beds.) Pre-registration HOUSE OFFICER in General Surgery. Vacant early September.

Applications to the Hospital Secretary.

WOLVERHAMPTON. NEW CROSS HOSPITAL. (634 Beds.) Pre-registration HOUSE OFFICER in Medicine. Vacant 1st October, 1957.

Applications to the Hospital Secretary.

WARRINGTON GENERAL HOSPITAL. (344 Beds.) Applications are invited for the post of SENIOR HOUSE OFFICER (pædiatrics), Male or Female. Post recognised for D.C.H. The post will become vacant on 1st October, 1957. Scale of salary £819 10s. p.a., less a deduction of £150 p.a. for residential emoluments.

Applications to be forwarded to—

HENRY L. BOOT, Group Secretary,
Warrington and District Hospital Management Committee.
c/o General Hospital, Warrington, Lancs.

NORTHERN IRELAND HOSPITALS AUTHORITY. Applications are invited for a whole-time appointment of TUTOR/REGISTRAR in Therapeutics and Pharmacology at hospitals managed by the Belfast Hospital Management Committee. The appointment will be made jointly by the Authority and the Queen's University, Belfast, and will involve teaching and other University duties as Tutor in the Department of Therapeutics and Pharmacology. The department has charge of beds at the above hospitals.

Applications should be made on a form which may be obtained (with further particulars) from the Secretary, Northern Ireland Hospitals Authority, 44–46, Queen-street, Belfast, and which must be returned so as to be received not later than 7th September, 1957.

B.W.I. UNIVERSITY COLLEGE HOSPITAL OF THE WEST INDIES. Applications are invited for the post of REGISTRAR in the Division of Surgery at the above-named Teaching Hospital. The successful candidate will be required to commence duty on or about 1st January, 1958. The appointment will be for 1 year in the first instance subject to renewal. Salary will be within the scale £900–£100–£1100/£1200–£100–£1500 p.a. depending on experience and qualifications. If available, an unfurnished flat will be provided at a deduction of 5% of salary, otherwise a living-out allowance will be paid by the Board. Return passages by sea will be paid for 1 person only from and to the country of recruitment.

Further information may be obtained from the Hospital Manager and Secretary, University College Hospital of the West Indies, Mona P.O., Jamaica, B.W.I., to whom application, stating age, nationality, details of qualifications and experience together with 3 recent testimonials or the names and addresses of 3 referees, should be sent by 21st September, 1957.

SOUTH AFRICA. DONALD FRASER HOSPITAL, SIBASA, NORTHERN TRANSVAAL. Applications are invited for the post of ASSISTANT MEDICAL OFFICER in the above Mission Hospital. Applicants must be interested in the physical and spiritual welfare of the African staff and patients. Salary scale £825–£75–£900–£100–£1000–£50–£1250, plus £200 cost-of-living allowance. Previous experience will be taken into consideration in determining commencing salary. The Hospital has 180 Beds and is planning to add another 100 beds for patients suffering from tuberculosis. There are 2 well-equipped operating theatres and an X-ray plant.

Applications, giving details of age, experience and qualifications, together with the names and addresses of 2 referees, should be addressed to the Medical Superintendent, Donald Fraser Hospital, P.O. Vhufuli, Via Sibasa, Northern Transvaal, South Africa.

U.S.A. CAMBRIDGE, MASSACHUSETTS. Applications are invited for the positions of RESIDENCIES in Anesthesia for a 2-year period beginning 1st July and 1st September, 1957. Salary $1800 first year and $3600 second year and full maintenance. Training in all branches of anesthesia. Affiliation with other hospitals.

Applications, stating age, nationality, qualifications, and experience, together with the names of their referees, should be forwarded to the Director of Anesthesiology, P.O. Box 89, Cambridge, Massachusetts. Travelling expenses to and from the U.S.A. will be paid. Particulars will be sent as soon as application is received. Please enclose recent photograph with application.

Public Appointments

FACTORY DOCTORS. Factories Acts, 1937 and 1948. The following appointment as Appointed Factory Doctor is vacant. Apply to Chief Inspector of Factories, 19, St. James's-square, London, S.W.1.

District	*County*	*Latest date for receipt of applications*
HASLEMERE	.. SURREY ..	.. 7TH SEPTEMBER, 1957

GOVERNMENT OF THE FEDERATION OF RHODESIA AND NYASALAND. MINISTRY OF HEALTH. Applications are invited for appointment as JUNIOR RESIDENT MEDICAL OFFICERS in Government Hospitals in the Federation with salary of £69 3s. 4d. per mensem.

Application forms and further particulars from Secretary (R), Rhodesia House, 429 Strand, London, W.C.2. Closing date 21st September, 1957.

LAGOS TOWN COUNCIL, Nigeria. Assistant Maternity AND CHILD WELFARE OFFICER (Male or Female) required by above Council on contract for 5 years in first instance. Salary scale (including inducement allowance) £1170 rising to £2118 a year, plus Staff pay £100 a year. Commencing salary according to qualifications and experience. Free passages for Officer and wife. Assistance towards cost of children's passages and grant up to £150 annually towards maintenance in United Kingdom. Liberal leave on full salary after each tour of 12–24 months. Outfit allowance £60 usually payable. Candidates must be registered medical practitioners and should preferably have postgraduate experience and/or training in obstetrics.

Write to the Crown Agents, 4, Millbank, London, S.W.1. State age, name in block letters, full qualifications and experience, and quote M3/43058/LD.

CITY OF NAIROBI. Appointment of Assistant Medical Officers (Male). The City Council of Nairobi is commencing a clinical service for the African population. 4 centres will be provided for the treatment of the ambulant sick for 24 hours per day. Applications are invited for the posts of :—

(I) ASSISTANT MEDICAL OFFICER (Grade I).
The appointment is a permanent established post and the consolidated salary scale is £1985–£60–£2345 p.a. This officer will be in administrative charge of the service under the direction of the Medical Officer of Health. He will also have to do general clinical work. Preference may be given to a person with administrative experience.

(II) ASSISTANT MEDICAL OFFICER (Grade II).
The appointment is a permanent established post and the consolidated salary scale is £1635–£50–£2085 p.a. The duties of this officer will be mainly whole-time clinical, but he will be expected to assist if necessary with the administration of the service.

Specialist medical qualifications are not necessary for either post but good all-round experience is desirable. Some flexibility in the staffing arrangements of this department is essential, and these doctors may be required to assist in the work of other sections. Such arrangements will play a minor part in time and general service. A knowledge of Swahili is not essential but the person appointed will be expected to have a good knowledge of the language within 6 months. Applicants should state clearly whether they are applying for the post of Assistant Medical Officer (Grade I) or Assistant Medical Officer (Grade II) and applicants for the Grade I post should state whether they wish to be considered for the Grade II post should their applications for the Grade I post be unsuccessful. The successful applicants will be required to pass a medical examination before appointment.

Application forms, together with a summary of main terms and conditions of service applicable to the appointment, are available on request from the East African Office, Grand Buildings, Trafalgar-square, London, W.C.2, and applications on such forms should be addressed endorsed "Application for Employment" so as to reach the Establishment Officer, P.O. Box 30037, Nairobi, Kenya, not later than 19th September, 1957. Canvassing, either directly or indirectly, will be a disqualification. JOHN RISEBOROUGH, Town Clerk.

P.O. Box 30075, Nairobi, 12th August, 1957.

DUBLIN. LOCAL APPOINTMENTS COMMISSION. Position vacant. BACTERIOLOGIST under the Board of Public Assistance for the South Cork Public Assistance District. Essential qualifications include the M.D., M.Sc., D.Sc., M.R.C.P.I. or equivalent. Upper age limit 50 years, with extensions in certain cases. Salary scale £1182–£1821. The person appointed may undertake, if offered, a University teaching appointment.

Application forms and particulars from the Secretary, 45, Upper O'Connell-street, Dublin. Latest time for receiving completed application forms 5 P.M. on 10th September, 1957.

STAFFORDSHIRE COUNTY COUNCIL. Health Department. Appointment of COUNTY PSYCHIATRIST. Applications are invited from registered medical practitioners with suitable experience to undertake duties involving the day-to-day control of the Mental Health Section of the Department, including mental deficiency and lunacy, together with child guidance arrangements of the School Health Service. Practical experience of child guidance work is desirable and the possession of a Diploma in Psychological Medicine will be considered an advantage. The candidate will be on the staff of the County Medical Officer of Health, to whom he will be responsible. The salary scale will be in accordance with the latest Industrial Court award—i.e., £1520 p.a., rising by annual increments of £50 (1) and £55 (7) to £1955 p.a., and previous similar service may be taken into consideration when deciding the commencing rate. The candidate appointed will be required to provide a car and will be paid allowances in accordance with the County Council's scale. The appointment, which will be terminable by 3 months notice in writing on either side, will also be subject to the provisions of the appropriate Superannuation Acts and Regulations, in which connection the successful candidate will be required to pass a medical examination and produce his or her birth certificate.

Applications, stating age, qualifications, and experience, together with copies of not more than 3 recent testimonials, should reach the County Medical Officer of Health, County Buildings, Stafford, not later than 13th September, 1957. Canvassing, directly or indirectly, will disqualify, and all applicants must state whether, to their knowledge, they are related to any member or senior officer of the County Council.

T. H. EVANS, Clerk of the County Council.

County Buildings, Stafford, 12th August, 1957.

WESTERN AUSTRALIA. STATE PUBLIC SERVICE. MENTAL HEALTH SERVICES. MEDICAL SUPERINTENDENT.

Salary : £A3070 (gross) p.a., plus £A100 if in possession of a Diploma in Psychiatry.

Qualifications : Applicants must possess a medical degree registrable in Western Australia ; have sound clinical experience and administrative ability ; a higher medical qualification is desirable.

Duties : Administrative and clinical control of Claremont Mental Hospital and the Reception Hospital at Claremont.

Accommodation : Free furnished residence, fuel, and laundry or an allowance in lieu.

Transport : A reasonable amount will be allowed for transport of appointee and dependent family to Western Australia provided a bond is entered into to serve the State for a period of 3 years.

Conditions of Service : Superannuation benefits, long service and annual leave, cumulative sick leave, and other conditions applicable to permanent public servants.

Further particulars from the Official Secretary, Agent General for Western Australia, Savoy House, 115, Strand, London, W.C.2, to whom applications, in duplicate, stating age, marital state, qualifications, experience, and 2 recent references and referees, should be addressed by 30th September, 1957.

NOTTINGHAMSHIRE COUNTY COUNCIL. Public HEALTH DEPARTMENT. Applications invited from registered medical practitioners (either sex) for either of the following whole-time appointments :—

SENIOR CLINICAL MEDICAL OFFICER. Salary within the scale £1250–£50–£1400–£55–£1510–£65–£1575, subject to a maximum commencing salary of £1400 p.a. Applicants should : (*a*) possess the D.P.H., D.C.H., or comparable qualification ; (*b*) have had at least 3 years experience as whole-time Clinical Medical Officer in the Ante-Natal, Child Welfare and School Health Services of a Local Authority since July, 1948 ; (*c*) have been approved by the Ministry of Education for, and have had substantial experience in, the ascertainment of educationally subnormal children.

ASSISTANT COUNTY MEDICAL OFFICER. Salary £1050–£50–£1200–£55–£1475, or, if holding a Diploma in Public Health, £1200–£55–£1475.

Application forms and conditions of appointment from the County Medical Officer, County Hall, Trent Bridge, Nottingham. Applications by 21st September, 1957.

A. R. DAVIS, Clerk of the County Council.

WEST HARTLEPOOL. COUNTY BOROUGH OF WEST HARTLEPOOL. Applications are invited for the appointment of DEPUTY MEDICAL OFFICER OF HEALTH AND DEPUTY PRINCIPAL SCHOOL MEDICAL OFFICER from registered medical practitioners possessing the Diploma in Public Health or similar qualifications. Candidates should have experience in the ascertainment of educationally subnormal pupils and preferably be approved by the Ministry of Education for this purpose. The officer appointed will be required to carry out such duties as shall be allocated from time to time by the Medical Officer of Health. The salary scale applicable to the post is £1396 p.a., rising by yearly increments of £52 10s. to a maximum of £1606 p.a. Previous service with a local authority will be taken into account in fixing the commencing salary within this scale. A car allowance of £75 p.a. has been paid to the present holder of the post. The appointment will be terminable by 3 months notice in writing on either side. The successful applicant will be required to pass a medical examination.

Applications, giving full details of the applicant's age, experience, and qualifications, together with names and addresses of 3 referees, should be sent to reach the Medical Officer of Health, Durham House, Victoria-road, West Hartlepool, not later than Saturday, 7th September, 1957.

ERIC J. WAGGOTT, Town Clerk.

Municipal Buildings, West Hartlepool, 7th August, 1957.

WINDWARD ISLANDS. District Medical Officer required for general hospital duties in Grenada. Appointment carries liability to serve in or transfer to any part of the Windward Islands. Candidates must possess qualifications registrable in United Kingdom. Appointment on permanent basis with pension (non-contributory) or agreement for 3 years. Salary scale £800–£1000 p.a. Pension 1/600th of final pensionable emoluments for each completed month of service. Private practice if duties permit or non-pensionable allowance of £100 p.a. in lieu. Income-tax at local rates. Pay addition of 20% of basic salary also payable. Unfurnished quarters provided at rental not exceeding 10% of salary. Free passages for Officer and family up to 5 persons in all. Generous leave.

Application forms from Director of Recruitment, Colonial Office, London, S.W.1 (quoting No. BCD. 117/41/01).

General Practice

For an ***Executive Council post*** *(England and Wales) apply on form* **E.C.16A** *obtainable from the council. Mark envelope "Vacancy."*

BOLTON, LANCASHIRE. Applications invited for medical practice VACANCY (urban) due to death. List at present approximately 2200. Intermediate area. Residence and surgery available for purchase. Apply on Form E.C.16A, before 31st August, 1957, to—

P. R. SCOWCROFT, Clerk of the Bolton Executive Council. Central Hall, 9, Acresfield, Bolton.

KIDDERMINSTER, WORCESTERSHIRE. Urban VACANCY due to death of female practitioner. List approximately 1400 (60% female). Closing date 31st August, 1957.

E.C.16A and full written details from the Clerk, Worcestershire Executive Council, 29, Foregate-street, Worcester.

SOUTH SHIELDS. Applications are invited for Vacancy (urban). List at present approximately 1600. Surgery available but not residence. Apply on E.C.16A to undersigned before 4th September, 1957.

A. WALLER, Clerk of the Executive Council.

2, Keppel-street, South Shields, Co. Durham.

BERMUDA. Owing to sudden death, Vacancy exists in Group practice for a Consultant Surgeon with considerable experience in general surgery with higher qualifications. Age 35–45. Excellent salary offered.

Reply with (1) full particulars, (2) names of 3 referees, and (3) recent personal photograph to BERMUDA MEDICAL ASSOCIATES, c/o Bermuda Travel Information Office, 6, Lower Regent-street, London, W.1, within 10 days of advertisement appearing. Personal interviews will be conducted in London and Glasgow where full details will be available.

Miscellaneous

The Rank Organisation Medical Service requires a whole-time Male Doctor, to take medical charge of Pinewood Studios, The Rank Laboratories, Denham, and Olympic Laboratory, Acton. The salary will be in accordance with the British Medical Association scale for an Assistant Medical Officer or Medical Officer, according to qualifications and experience.

Further particulars from the Consulting Physician, THE RANK ORGANISATION LTD., 11, Belgrave-road, London, S.W.1.

Abbott Laboratories Limited, international manufac-turers of fine pharmaceuticals wish to appoint a Medical Director, with the following responsibilities :—

(1) Clinical research—the initiation of clinical trials of new products by the medical profession, the analysis of reports received and the incorporation of the information so received into medical literature.

(2) Professional relations between Abbott and the medical profession including all correspondence of a medical nature.

(3) Consultant to the research and pharmaceutical development departments in the initiation of new products.

(4) Consultant to the sales, advertising, production and quality control departments on all medical matters.

Candidates aged between 35 and 45 years should have, in addition to a medical degree, either (*a*) a postgraduate degree in 1 of the basic sciences, or Membership, with 4–5 years medical practice, or (*b*) at least 3 years hospital appointments with some background of clinical research, plus 4–5 years experience in hospital practice. This strong scientific and medical basis is essential, but a sound commercial sense will also be an important quality in order to effect a smooth coördination of the various aspects of the Company's business. Candidates with some few years of hospital or University teaching experience, especially in the postgraduate field, will have an advantage. The position will call for fairly extensive travel within the United Kingdom. The starting salary will be not less than £2500 p.a.

Candidates are invited to write, in confidence, full details of their career to date, to the Managing Director, ABBOTT LABORATORIES LIMITED, 3, Wadsworth-road, Perivale, Greenford, Middlesex.

Parke, Davis & Company, Limited, invite applications for the post of Director of Pharmacological Research in their new biological laboratories, which will be completed during the late summer of 1958.

The position is one that requires creative ability and qualities of leadership, and applicants should have high academic qualifications in both physiology and pharmacology ; a medical qualification would be an advantage.

The Company has long experience in the field of fundamental research into new drugs and the Director will be expected to initiate and direct work of this kind, in addition to supervising the more routine screening programmes.

There is a generous pension and life assurance plan.

Applications for this post, which carries an appropriately high salary, should be made to the Deputy General Manager, PARKE, DAVIS & COMPANY, LIMITED, Staines-road, Hounslow, Middlesex.

A Swiss Pharmaceutical Company with an international reputation desires to appoint a British Medical Practitioner to their Medical Advisory Staff in Basle. Candidates should speak German and have a strong interest in clinical research in order to maintain a liaison in medical matters with certain English-speaking countries. Terms and conditions of employment would be open to discussion but commencing remuneration would not be less than £1700 p.a.

Applicants should state complete particulars of experience and qualifications, which will be regarded in strict confidence, to Address, No. 325, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Physician (pathological and neurological experience required) for clinical and research work. Salary range $6500–$9500 p.a.—Detailed personal and professional data, mail to Clinical Director, Box 144, Wrentham, Massachusetts, U.S.A.

Scotland. Partnership with view to eventual succession required by experienced Scottish G.P. at present principal in England. Replies treated as confidential.—Address, No. 324, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Partnership required, London or Home Counties. Experi-enced Practitioner. Ample capital house purchase.—Address, No. 326, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Leading South Coast Resort. Lease, equipment and good-will of old-established nursing-home for sale. Midwifery, medical and convalescent. 13 single and 1 double bedroom (all basins h. and c.), 3 bathrooms, 5 w.c.'s. 2 floors only. Esse cooker in kitchen. Central heating. 2 garages with flat over. Lease 16 years at a rental of £612 p.a. inclusive of rates and use of antique furniture in beamed drawing-room. Audited account. Price £3850.—Particulars in confidence from Owners' Agents, HEFFORD & HOLMES, F.A.I., 51, Gildredge-road, Eastbourne (Tel. 7840).

Wanted, second-hand vertical chest screening unit.—Address, No. 323, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

"Pregnancy Diagnosis by the Xenopus Method," 24-hour service. Send specimens of urine and £1 1s. fee. Hæmatology, Biochemistry, Flame Photometry.—WELBECK BIOLOGICAL LABORATORIES, 26, Park-crescent, Portland-place, W.1 (MUSeum 5386–7).

Applicants for posts requiring testimonials copied or duplicated should communicate with MANTON SECRETARIAL SERVICE LTD., 98, Victoria-street, S.W.1 (Phone : VICtoria 0141), who are specialists in this kind of work.

Typewriting and Duplicating. First-class work at moder-ate prices by experienced medical typists. Electric machines. —SYBIL RANG, 21, Heath-street, Hampstead, London, N.W.3 (HAM 5329/0504).

Translations of medical articles, &c., German-English, English–German.—Address, No. 322, THE LANCET Office, 7, Adam-street, Adelphi, London, W.C.2.

Dr. Frederick Wesley Prigg Clutterbuck, formerly of 61, Clifton-road, Greenford, Middlesex, is asked to communicate with ARTHUR W. KEMP, Esq., Solicitor, Town Hall Chambers, 374/8, Old-street, London, E.C.1.

PUBLISHED by the PROPRIETORS, THE LANCET LIMITED, 7, Adam Street, Adelphi, in the County of London.
Printed by HAZELL, WATSON & VINEY, LTD., London and Aylesbury—Saturday, August 24, 1957.
PRINTED IN GREAT BRITAIN—Entered as Second Class at the New York, U.S.A., Office.

A LONG-ACTING INHIBITOR OF GASTRIC SECRETION

Compound I.S. 499

This compound was recently reported* to be a promising drug for reducing gastric secretion, especially at night, in patients with peptic ulcer. It is now undergoing clinical trial.

Compound I.S. 499 has a prolonged action with few, if any, side effects in therapeutic dosage.

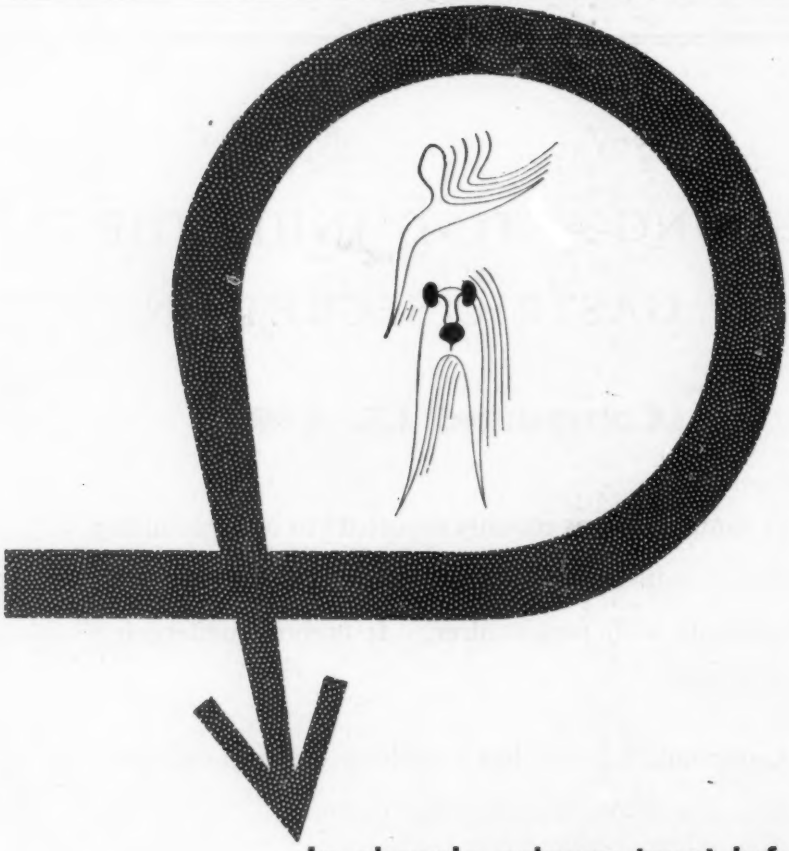
**Brit. med. J.*, ii : 275, 1957

Consulting physicians and others engaged in hospital practice can receive further information and supplies for controlled clinical trials by writing to :

THE MEDICAL LIAISON OFFICER

C. L. BENCARD LTD.

Park Royal, London, N.W.10.



In chronic urinary tract infections

General malaise, backache, shivers, abnormalities in micturition—such symptoms often point to chronic pyelitis.
Mandelamine is eminently suited to the long term treatment of urinary tract infections. It is bactericidal and bacteriostatic for a wide range of pathogens, particularly B. coli and Streptococcus faecalis.
Mandelamine is non-toxic and virtually free from side-effects, and is safe for prolonged administration. It does not give rise to resistant strains.

DOSAGE

Adults Two Hafgrams three times a day.
Children One 0.25 G. tablet three times a day.
Infants Less than one year old, one 0.25 G. tablet twice a day.

PRESENTATION

Mandelamine Hafgrams (0.5 G.) Bottles of 30, 250 and 500.
Mandelamine Tablets (0.25 G.) Bottles of 60, 500 and 1000.

MANDELAMINE HAFGRAMS

Trade Mark

WARNER

WILLIAM R. WARNER & CO. LTD., EASTLEIGH, HAMPSHIRE

HAN 372/4